Stereoselective Synthesis of 2-Deoxy-2-Iodo-*O*-Glycoside in Biphasic Medium and BDMS Mediated Facile Access to *2,3-Unsaturated-O-Glycoside, Imidazopyridine and α-Aminoamidine*

A Dissertation Submitted to the
Indian Institute of Technology Guwahati
As Partial Fulfillment for the Degree of

DOCTOR OF PHILOSOPHY

by

R. Sidick Basha
Roll No. 09612214

Department of Chemistry
Indian Institute of Technology Guwahati
Guwahati-781 039
July 2014

'The Unique Challenge which Chemical Synthesis provides for the Creative Imagination and the skilled hands ensure that it will endure as long as men Write books, Paint pictures, and Fashion things which are beautiful, or practical, or both

R. B. Woodward

STATEMENT

I do hereby declare that the matter embodied in this thesis entitled "*Stereoselective Synthesis of 2-Deoxy-2-Iodo-O-Glycoside in Biphasic Medium and BDMS Mediated Facile Access to 2,3-Unsaturated-O-Glycoside, Imidazopyridine and α-Aminoamidine*" is the result of investigations carried out by me under the supervision of Prof. Abu T. Khan in the Department of Chemistry, Indian Institute of Technology Guwahati, India.

In keeping with the general practice of reporting scientific observations, due acknowledgements have been made wherever the work described is based on the findings of other investigators.

IIT Guwahati
August 08, 2014

R. Sidick Basha

Indian Institute of Technology Guwahati
Guwahati – 781039, India
Tel. No.: +91-361-2582305
Fax No.: +91-361-2582349
e-mail: atk@iitg.ernet.in

Dr. Abu T. Khan
Professor of Chemistry

CERTIFICATE

This is to certify that Mr. R. Sidick Basha has been working in my research group since January, 2011 as a regular registered Ph. D. student. I am forwarding his thesis entitled "*Stereoselective Synthesis of 2-Deoxy-2-Iodo-O-Glycoside in Biphasic Medium and BDMS Mediated Facile Access to 2,3-Unsaturated-O-Glycoside, Imidazopyridine and α-Amino amidine*" being submitted for the Ph. D. (Science) Degree of this Institute. I certify that he has fulfilled all the requirements according to the rules of this Institute regarding the investigations embodied in his thesis and this work has not been submitted elsewhere for a degree.

IIT Guwahati
August 08, 2014

Prof. A. T. Khan
(Thesis Supervisor)

Indian Institute of Technology Guwahati
Guwahati – 781039, India
Tel. No.: +91-361-2582307
Fax No.: +91-361-2582349
e-mail: patel@iitg.ernet.in

Dr. Bhisma K. Patel
Professor and Head
Department of Chemistry

CERTIFICATE

This is to certify that Mr. R. Sidick Basha has completed his Ph. D. Thesis work from 01 January, 2011 as a regular registered Ph. D. student under my colleague Prof. Abu T. Khan. I have been appointed as a Co-Supervisor when Prof. Khan joined as Vice-Chancellor of Aliah University in West Bengal on deputation from IIT Guwahati. I am forwarding his thesis as a Co-supervisor entitled "*Stereoselective Synthesis of 2-Deoxy-2-Iodo-O-Glycoside in Biphasic Medium and BDMS Mediated Facile Access to 2,3-Unsaturated-O-Glycoside, Imidazopyridine and α-Amino amidine*" being submitted for the Ph. D. (Science) Degree of this Institute. I also certify that he has fulfilled all the requirements according to the rules of this Institute regarding the investigations embodied in his thesis and this work has not been submitted elsewhere for a degree.

IIT Guwahati
August 08, 2014

Prof. B. K. Patel
(Thesis Co-Supervisor)

Acknowledgement

I would like to express my deepest gratitude to my research supervisor Professor Abu T. Khan for his valuable suggestion, perceptive guidance and decisive insights during the entire course of Ph.D. work. His Moral scientific spirit and ever-friendly nature has uplift me a lot during my research work which enrich my ideas. I am extremely thankful to him for giving me a liberty to pursue my own ideas and conceptual quest of knowledge toward research. I find myself privileged to have worked under his kind guidance. My endless gratitude goes towards him. I will always be grateful to my Co-supervisor Prof. B. K. Patel for providing me all sort of necessary vision and eternal support during absence of my Thesis Supervisor. I wish to convey my sincere gratitude to Prof. T. Punniyamurthy Chairman of Doctoral Committee, and other members Dr. B. Mandal, and Prof. V. V. Dasu for their intellectual support, encouragement and helpful suggestions. My genuine regards to all the faculty of the Department of Chemistry for their encouragement and inspiration.

I am grateful to Council of Scientific and Industrial Research (CSIR), India for financial support and IIT Guwahati for all the facilities that were made available to me. I extend my gratitude to Central Instrument Facility, IIT Guwahati for Instrument facility and DST for X-ray facility.

I wish to acknowledge Dr. Md. Musawwer Khan, Dr. Mohan Lal, Dr. Deb K. Das, Prasanta, Ajaz, Arindam, Satavisha, Kobirul, Suchandra, Belal, Karuna, Gattu and my other labmates for their direct and indirect help. I express my profound gratefulness to all friends from IITG for their help and encouragement. Special thanks to Dr. Babulal Das regard XRD data collection.

It is a great pleasure to express my gratitude to our staff of CIF Mr. Chandan Borgohain, Mr. Kula Kamal Senapati and Mr. Kh. Kesho Singh for their assistance and co-operation. I express my heartiest thanks to all the research scholars, Department of Chemistry, IIT Guwahati for their help and endless support.

I am grateful to Dr. Aiyagari Ramesh, Department of Biotechnology, IIT Guwahati and Suman Khan, Department of Chemical Science, Gauhati University for their necessary dissertation corrections.

I owe my sincere thanks to our technical staff Abhilasha, Lipika, Parikshit, Aniruddha, Diganta, Shyamal and office staff Nilyotpal, Imdadul, Santanu for their diplomatic help and professional support.

I am extremely grateful for the everlasting support, love and blessings from my Parents, who have always motivated me in all stages of my life.

R. Sidick Basha

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Abbreviations

Ac	acetyl
AIBN	azobisisobutyronitrile
BDMS	bromodimethylsulfonium bromide
Bn	benzyl
Boc	*tert*-butoxycarbonyl
Bu	butyl
t-Bu	*tert*-Butyl
Bz	benzoyl
CAN	cerium(IV)ammonium nitrate
Cbz	benzyloxycarbonyl
CCDC	Cambridge Crystallographic Data Centre
COSY	correlation spectroscopy
DCE	1,1-dichloroethane
DCM	dichloromethane
DMAP	*N*,*N*-4-dimethylaminopyridine
DME	dimethyl ether
DMF	*N*,*N*-dimethylformamide
DMSO	dimethylsulfoxide
EDCI	1-ethyl-3-(3-dimethylaminopropyl)carbodiimide
Et	ethyl
HFIP	hexafluoroisopropanol
IR	infrared
MCR	multicomponent reaction
Me	methyl
Mp	melting point
MS	molecular sieves
MW	microwave
NMR	nuclear magnetic resonance
NOESY	Nuclear Overhauser Enhancement Spectroscopy
i-Pr	isopropyl
Ph	phenyl

ppm	parts per million
Pr	propyl
p-TSA	*p*-toluenesulfonic acid
Py	pyridine
rt	room temperature
TBS	*tert*-butyldimethylsilyl
Tf	trifluoromethanesulfonyl
TFA	trifluoroacetic acid
THF	tetrahydrofuran
TLC	thin layer chromatography
TMS	trimethylsilyl
TMSOTf	trimethylsilyl trifluoromethanesulfonate

Chapter I

General Introduction to O-glycosylation of Sugars

1.1 Introduction

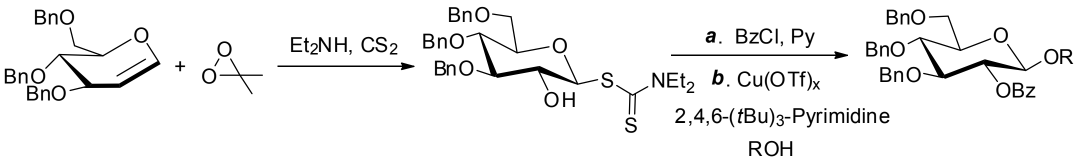
Carbohydrates play an essential role in living organism[1] and support a diverse array of biological functions. They are involved in storage of energy from natural resource of glycogen and starch, which lead to reliable materials as cellulose and proteoglycans.[2-4] Moreover, they reside in every cell surface in form of glycolipids and glycoproteins. They also acts as glycocode, depends on α or β glycosyl unit assembly. Carbohydrates possess a significant role in cell-cell interactions and cell communication for various biomedical investigations.[5-7] They also act as ligands for numerous regulatory processes.[8,9] A classical polysaccharide unit heparin[10] is found to be a potent anticoagulant. Carbohydrate-based drugs are found to be the most important pharmacophores due to their lack of toxicity and minimal immunogenicity. Carbohydrate-protein interactions in neoglycoconjugates help to analyze the functions of the glycan for targeted diagnostic medicines. Numerous methods have been developed for targeted glycovaccines and glycoconjugates. Carbohydrates such as glycans are also involved in many biological processes[11] such as cell and tumor growth, fertilization and tumor metastasis.

Carbohydrates interact with proteins through *O*-glycoside linkage and alter the biological process of conjugate in terms of stability and activity toward enzymes. It also governs the protein three-dimension orientation.[12] Oligosaccharides associate in many biological functions such as blood group determination, binding ability of lectins and hormone regulation.[13-15] Indeed, synthetic oligosaccharides exist as drugs in pharmaceuticals, and are usually achieved through glycosylation methods. The challenging task for synthetic chemist is to attain a lucid synthetic pathway for complex carbohydrate molecules. The significant problem in glycosylation is stereochemistry control at the anomeric centre (α or β configuration) followed by regioselective glycosylation using orthogonal protecting group. There are eight different classical methods used for glycosylation which is shown in Figure 1. Among them glycosylation on glucal assembly is highly desirable due to their diverse synthetic utility for the construction of natural products,[16] oligosaccharide[17] and *C*-glycosides synthesis.[18] In 1873, Michael[19] first synthesized a phenyl glucoside using acetobromoglucose and sodium phenoxide. Later on, Koenigs and Knorr[20] first demonstrated a silver based promoter[21] for controlled glycosylation from glycosyl halides. In the last decade, rapid growth on glycosylation synthesis has been achieved. However, till date there is no general method available for *O*-glycosylation.

Figure 1. Methods used for glycosylation

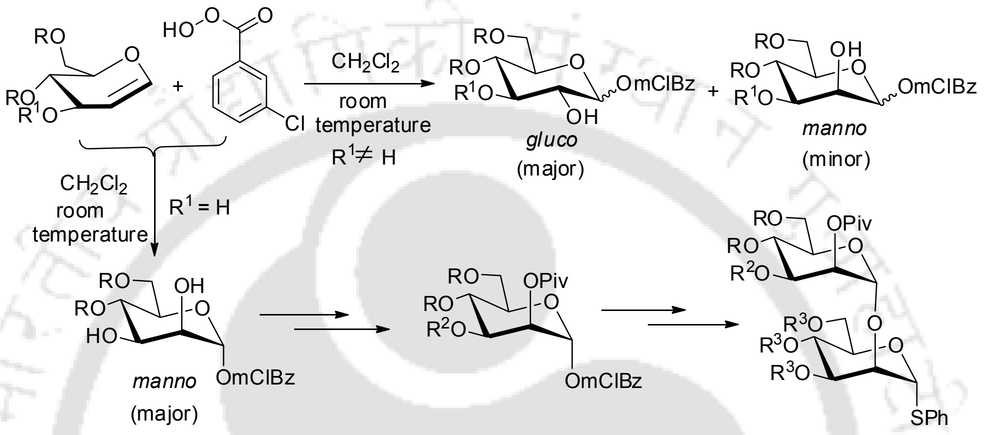
1.2 Synthetic Strategies and Development of *O*-Glycosylation on Glycal Assembly

Wei *et al.*[22] developed the stereoselective synthesis of β-*O*-glycoside from 3,4,6-tri-*O*-benzyl-ᴅ-glucal through *O*-glycosylation. In this methodology epoxyglycal reacts with diethylamine and carbon disulfide (CS_2) leading to *in situ* generation of glycosyl dithiocarbamates, which subsequently triggered by copper triflate along with acid scavenger 2,4,6-(*t*Bu)$_3$-pyrimidine forms β-*O*-glycoside as shown in Scheme 1.



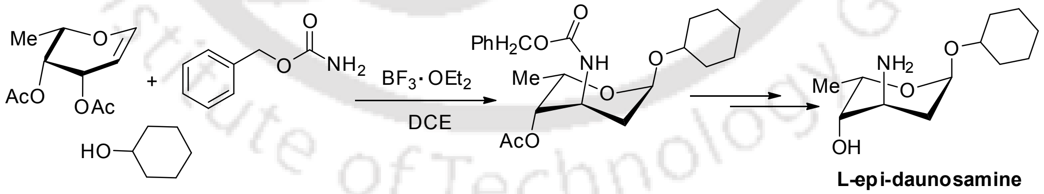
Scheme 1

Castillon *et al.*[23] reported that fully protected glucal react with MCPBA in dichloromethane at room temperature which attain a stereoselective glucopyranoside derivative. However, in case of 4,6-Di-*O*-protected glucal it led to mannopyranoside derivative. The corresponding mannopyranoside were further extended for the synthesis of complex disaccharide unit which is represented in Scheme 2.



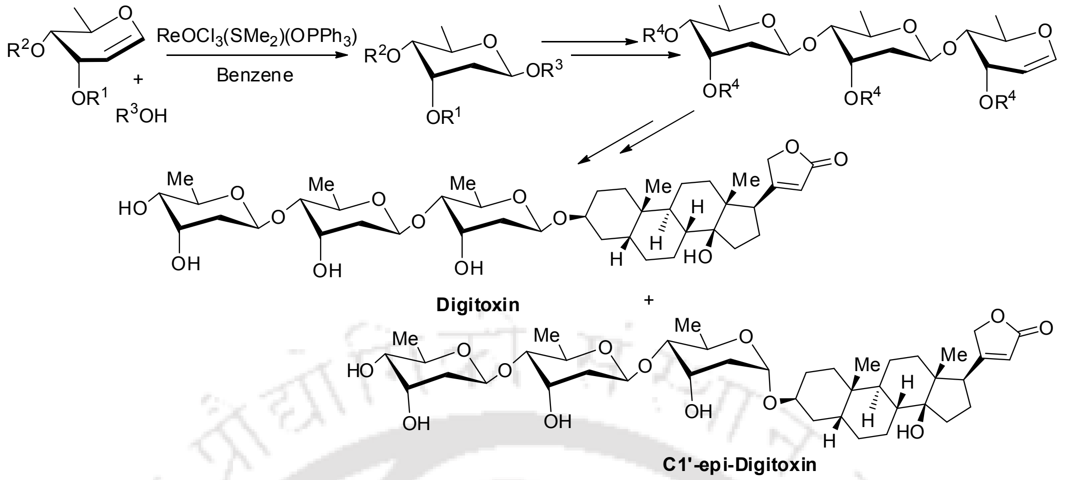
Scheme 2

Liu *et al.*[24] demonstrated that 3,4-di-*O*-acetyl-6-deoxy-L-galactal react with benzyl carbamate, cyclohexanol through *O*-glycosylation in presence of boron trifluoride as catalyst in DCE furnish to 3-amino-2,3,6-trideoxyhexoses, which subsequently underwent two more steps to achieve L-epi-daunosamine as shown in Scheme 3.



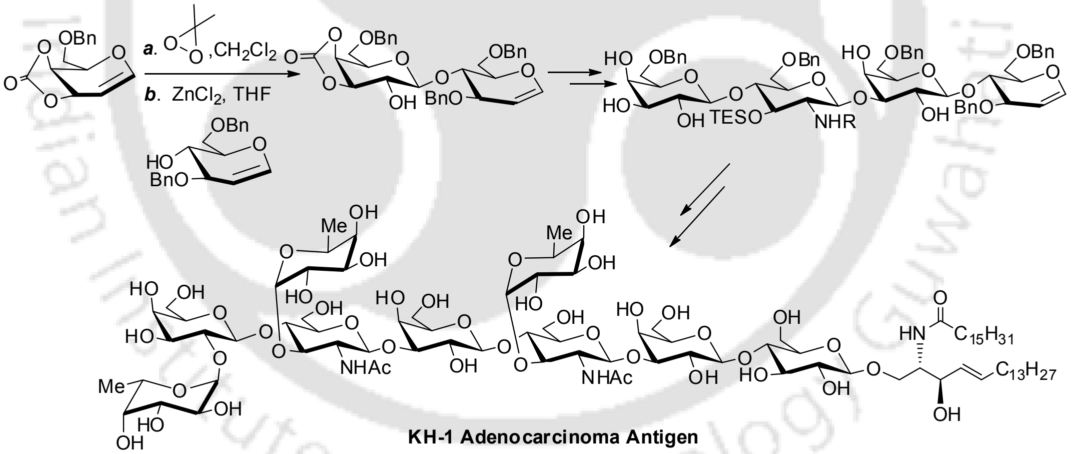
Scheme 3

Zhu *et al.*[25] developed a methodology wherein 6-deoxy-D-allal react with glycosyl donor in presence of rhenium(V) as a catalyst to afford stereoselective β-D-Digitoxosides. In addition to that, the method was further extended for the synthesis of Digitoxin and C1'-epi-Digitoxin which is shown in Scheme 4.



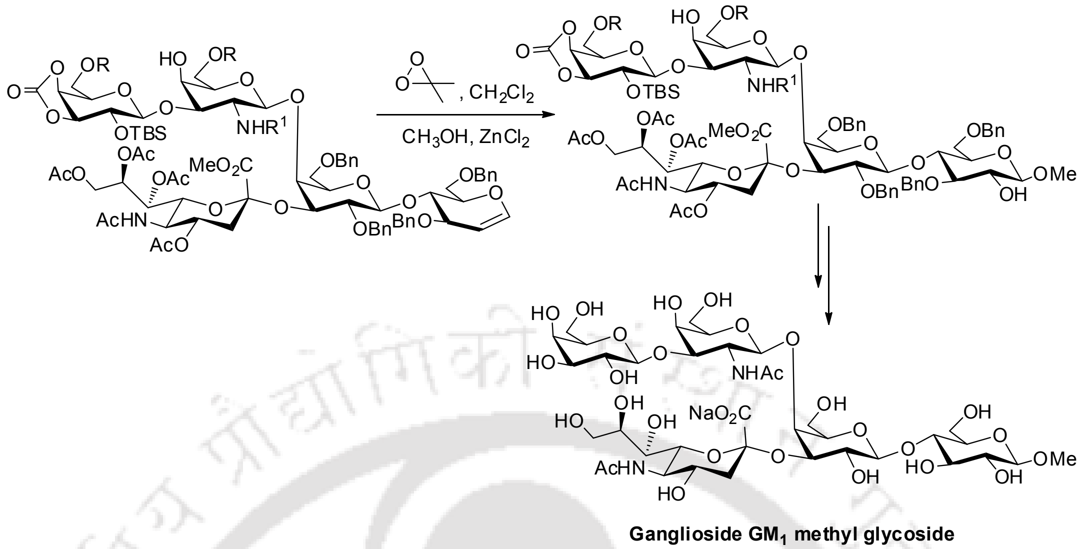
Scheme 4

Danishefsky *et al.*[26] demonstrated the total synthesis of KH-1 adenocarcinoma antigen, a potential anticancer vaccine by utilizing *O*-glycosylation on glucal assembly as a key synthetic intermediate step which is shown in Scheme 5.



Scheme 5

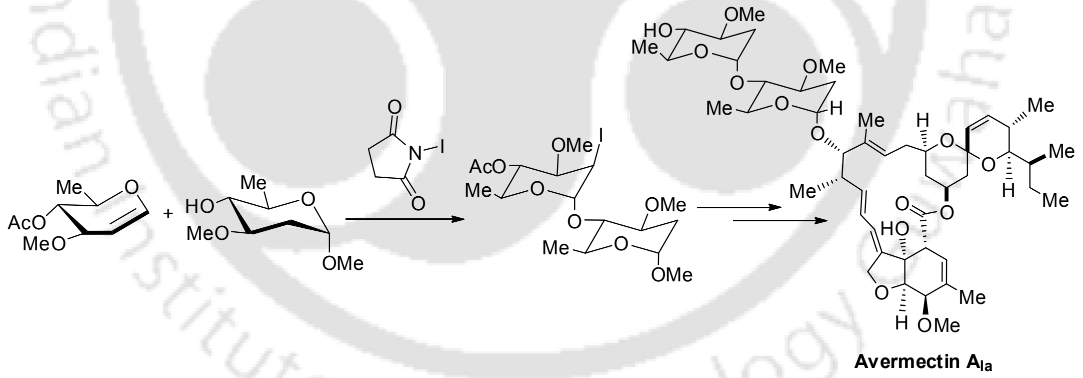
Pentasaccharide glucal moiety reacts with dimethyldioxirane/acetone in dichloromethane followed by zinc chloride in methanol leading to *O*-glycosylation of pentasaccharide, which subsequently undergoes several steps to attain the target molecule of Ganglioside GM_1 methyl glycoside[27] which is represented in Scheme 6.



Scheme 6

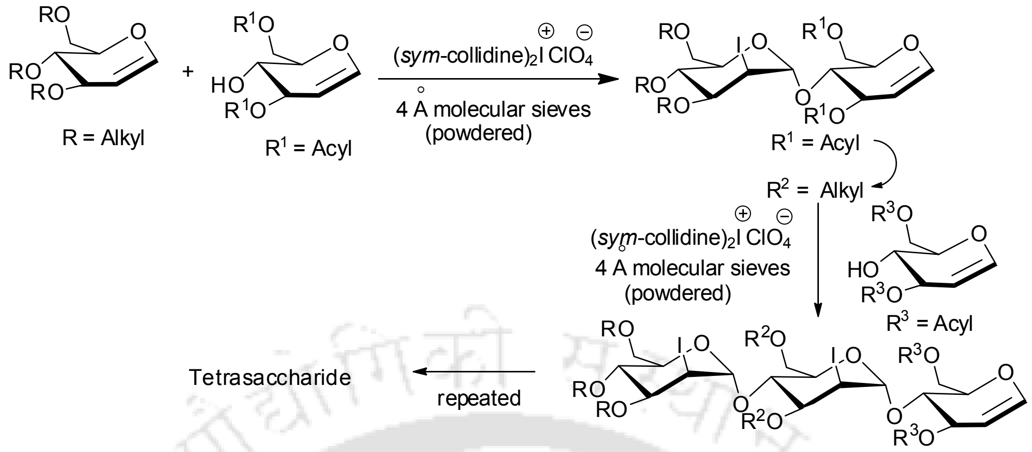
1.3 Synthetic Strategies and Development of Iodoglycosylation

Danishefsky *et al.*[28] demonstrated the total synthesis of Avermectin A_{1a} by utilizing Iodo glycosylation as a key step which is shown in Scheme 7.



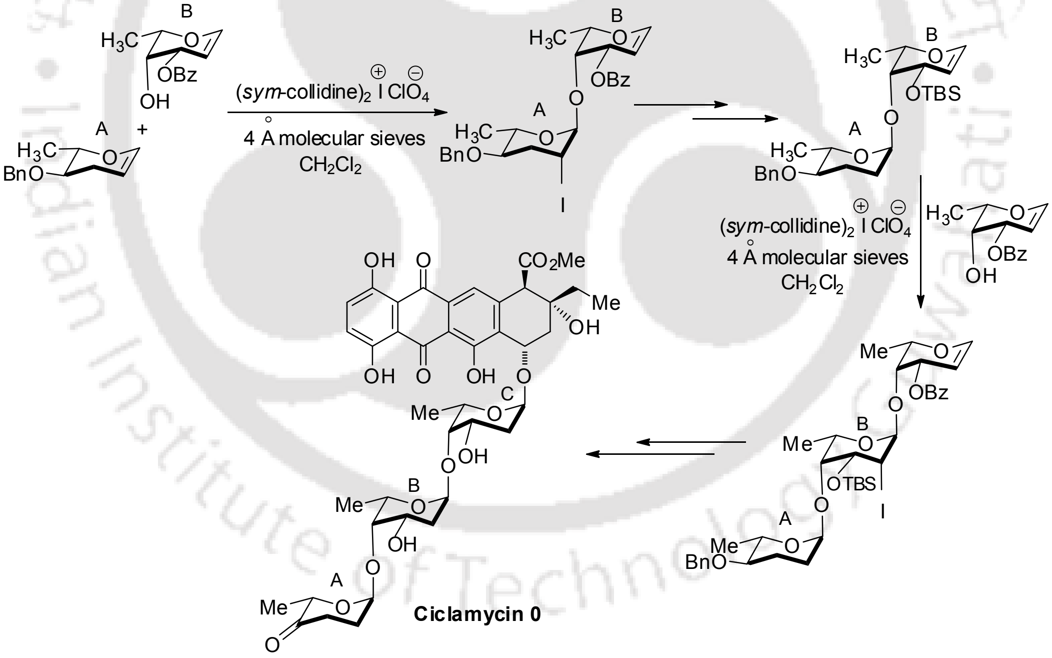
Scheme 7

Tetrasaccharide were synthesized from two different glucal moiety by using (*sym*-collidine)$_2$I$^+$ClO$_4^-$ as an iodinating agent.[29] The key fact of this methodology is that one of the glucal moiety which deactivate the ring in presence of an acetyl substituent led to controlled stereoselective iodoglycosylation which is shown in Scheme 8.



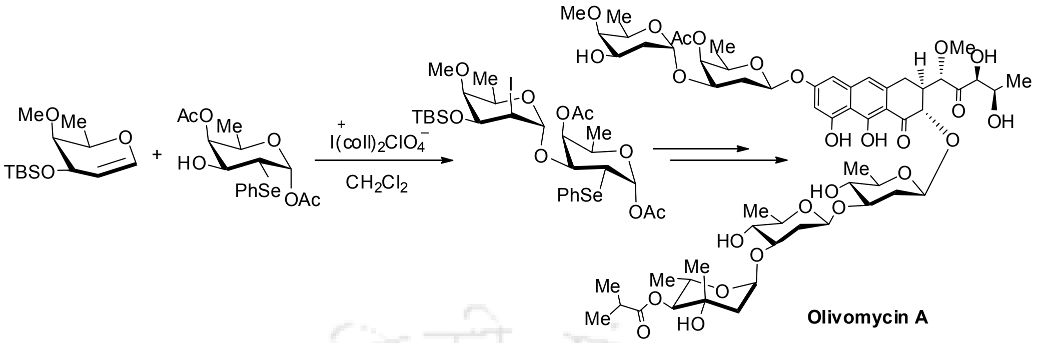
Scheme 8

Danishefsky *et al.*[30] achieved the total synthesis of ciclamycin 0 by using two stereoselective iodo-glycosylation as the key step *via* (*sym*-collidine)$_2$I$^+$ClO$_4^-$ as an iodinating agent as depicted in Scheme 9.



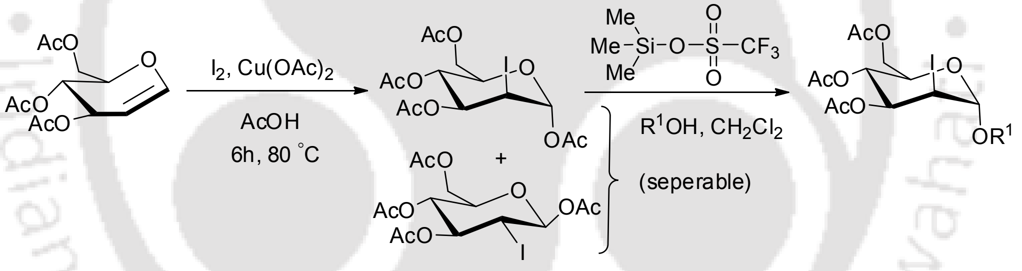
Scheme 9

Roush *et al.*[31] developed that mono silylated-ᴅ-fucal reacted with 3-hydroxy-galacto-2-phenylseleno acetate in presence of I$^+$(coll)$_2$ClO$_4^-$ in dichloromethane at room temperature leading to a stereoselective α-iodoglycosylation of β,α-disaccharide, which underwent several steps to attain the target molecule of olivomycin A which is represented in Scheme 10.



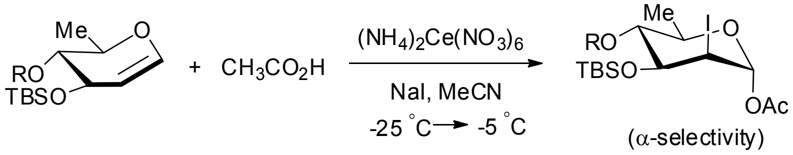
Scheme 10

Lafont *et al.*[32] demonstrated that 3,4,6-tri-*O*-acetyl-ᴅ-glucal react with acetic acid in presence of iodine/copper acetate which afford a separable 2-Iodo-β-glucopyranoside and 2-Iodo-α-mannopyranoside. Typically, the obtained 2-Iodo-α-mannopyranoside further undergoes reaction with alcohol, TMSOTf in dichloromethane to furnish alkyl-3,4,6-tri-*O*-acetyl-2-deoxy-2-iodo-α-ᴅ-mannopyranoside which is shown in Scheme 11.



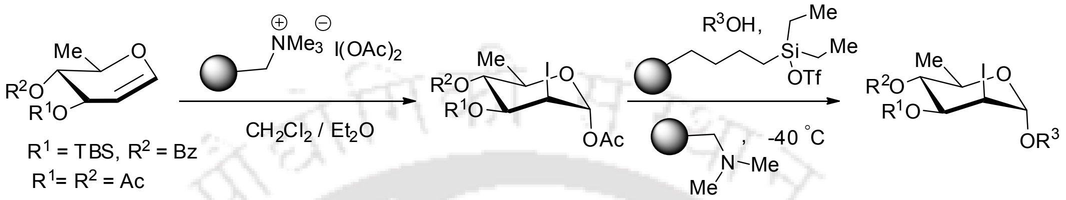
Scheme 11

Roush *et al.*[33] mentioned a stereoselective synthesis of 2-deoxy-2-iodo-mannopyranosyl acetates from glycal using ceric(IV) ammonium nitrate, sodium iodide and acetic acid in acetonitrile at -25 °C to -5 °C as shown in Scheme 12. The Major outputs of the results showed a superior selectivity than NIS in acetic acid.



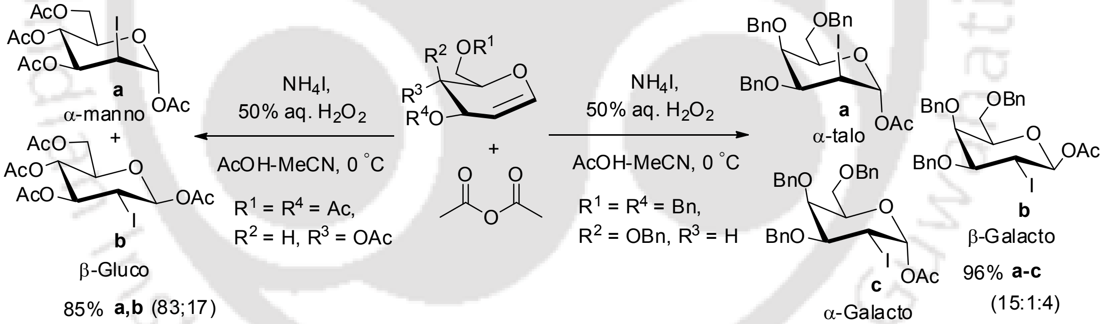
Scheme 12

Kirschning *et al.*[34] demonstrated that polymer-bound bis(acetoxy)iodate(I) reacted with glycal in dichloromethane/diethyl ether leading to 2-iodo-α-glycosyl acetates, which is activated by polymer-bound silyl triflate with different glycosyl acceptors at -40 °C to afford 2-deoxy-2-iodo-α-glycosides with a good yield which is shown in Scheme 13.



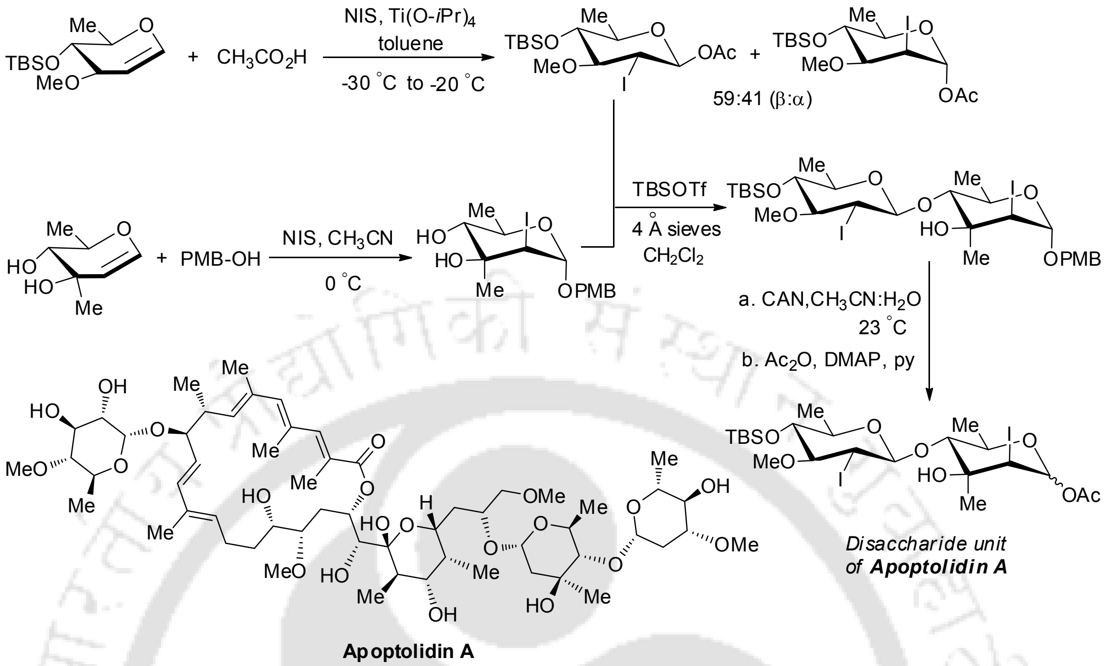
Scheme 13

Gammon *et al.*[35] developed a stereoselective synthesis of iodoacetoxylation from glucal using ammonium iodide, 50% aqueous H_2O_2 and Ac_2O/AcOH in acetonitrile at 0 °C. Moreover, in case of 3,4,6-tri-*O*-benzyl-ᴅ-galactal it afforded a mixture of *talo* and *galacto* pyranosides as depicted in Scheme 14.



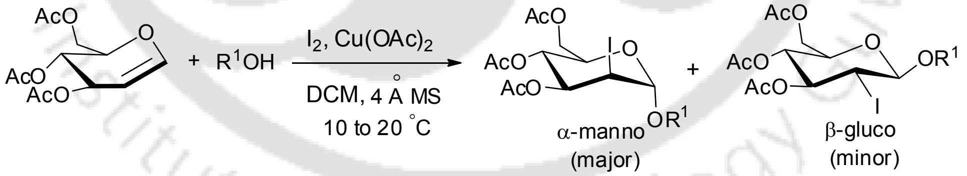
Scheme 14

Roush *et al.*[36] developed a disaccharide unit of Apoptolidin A via stereoselective synthesis of 2-iodo-β-glucopyranoside from glycal using NIS, Ti(O*i*Pr)$_4$ at -30 °C to -20 °C. Moreover, 3-*C*-methyl-ʟ-rhamnal reacts with *p*-methoxybenzyl alcohol in NIS at 0 °C leading to 4-hydroxy-3-*C*-methyl-2-iodo-α-mannopyranoside. The resulted 2-iodo-β-glucopyranoside react with acceptor 4-hydroxy-3-*C*-methyl-2-iodo-α-mannopyranoside in TBSOTf to furnish diiododisaccharide assembly, which further undergoes deprotection of *p*-methoxybenzyl group using CAN followed by protection of hydroxyl group by Ac_2O, pyridine to deliver the target molecule which is shown in Scheme 15.



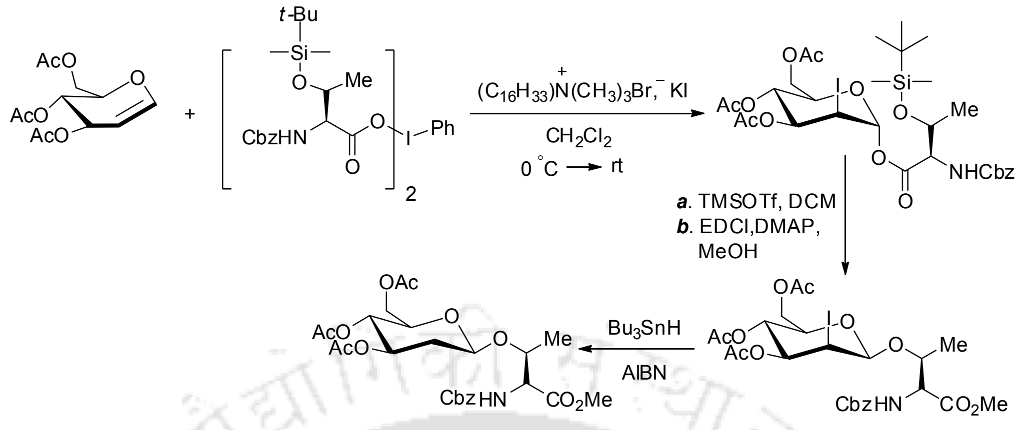
Scheme 15

Saeeng *et al.*[37] illustrated that 3,4,6-tri-*O*-acetyl-ᴅ-glucal reacted with variety of alcohol using I_2, $Cu(OAc)_2$ in dichloromethane at 10 to 20 °C direct to stereoselective synthesis of 2-deoxy-2-iodo-α-mannopyranoside as major one which is shown in Scheme 16.



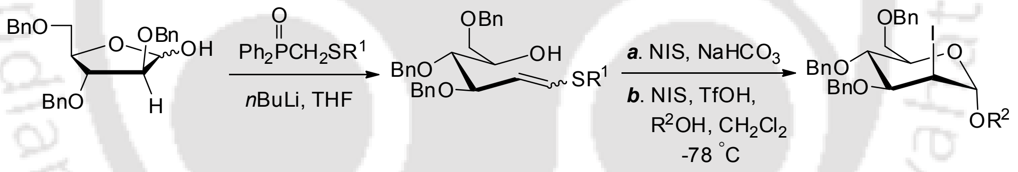
Scheme 16

Hotha *et al.*[38] demonstrated that 3,4,6-tri-*O*-acetyl-ᴅ-glucal react with $PhI(OCOR)_2$ in presence of CTAB, KI in dichloromethane at 0 °C to room temperature to afford 2-deoxy-2-iodo-α-mannopyranoside, which consequently involved in neighboring group participation in presence of Lewis acid leading to stereoselective β-iodo-mannopyranoside. However, the method was further extended for the synthesis of 2-deoxy-*O*-glycoside as shown in Scheme 17.



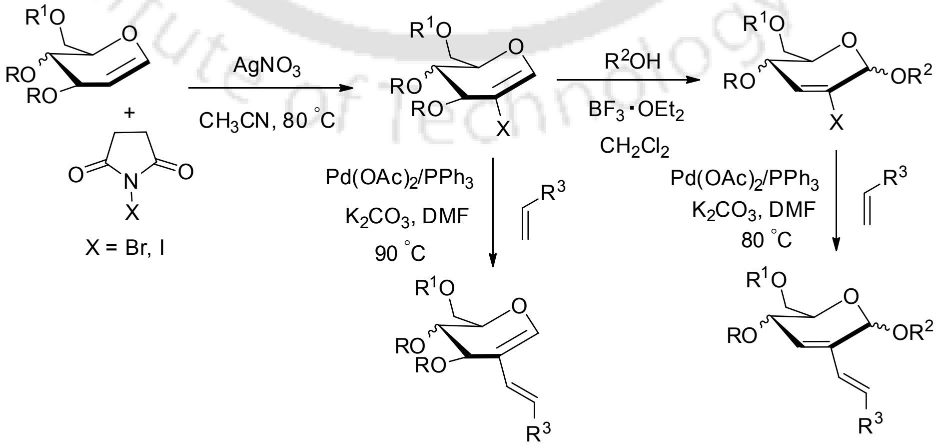
Scheme 17

Díaz and Boutureira *et al.*[39] represented the olefination reaction on 2,3,5-tri-*O*-benzyl-D-arabinofuranose using $Ph_2P(O)CH_2SR^1$ and *n*BuLi. The resulting open chain alkenyl sulfide react with NIS, $NaHCO_3$ promote I^+ endocyclization leading to 2-deoxy-2-iodo-1-thiomannopyranoside, which subsequently react with alcohol in NIS, TfOH at -78 °C to offer the stereoselective 2-deoxy-2-iodo-α-mannopyranosides which is shown in Scheme 18.



Scheme 18

Vankar *et al.*[40] demonstrated that glucal react with NIS/NBS, $AgNO_3$ in MeCN at 80 °C furnish to 2-iodoglycals/2-bromoglycals. The synthesized 2-haloglycal were further



Scheme 19

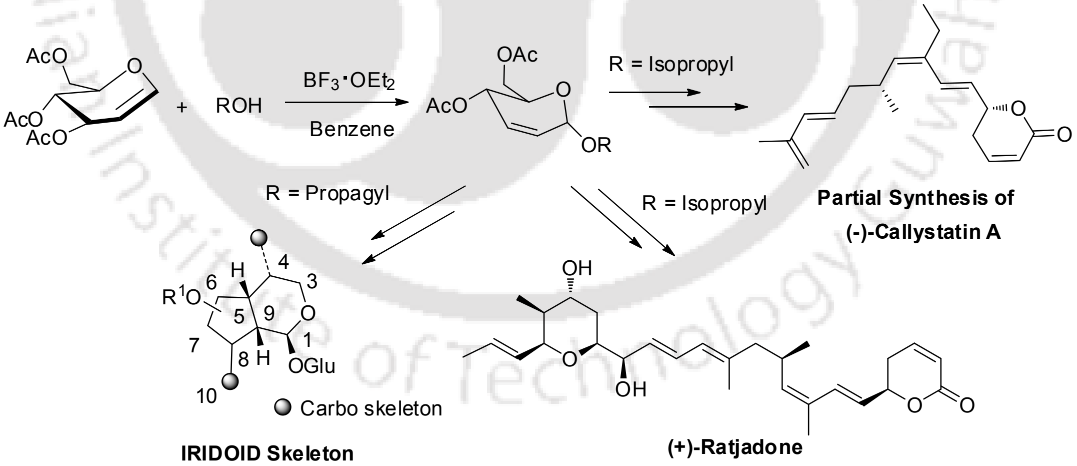
utilized for Heck coupling reaction which offered 2C branched glycals. In contrast to that, Ferrier reaction along with Heck coupling reaction resulted to 2C-branched-*O*-glycosides as represented in Scheme 19.

1.4 *Ferrier rearrangement Importance*

Ferrier rearrangement[41] was found to be an elegant approach for the synthesis of 2,3-unsaturated-*O*-glycosides, which reside as constructive subunit for several antibiotics.[42] Moreover, it is further utilized as glycosyl donors for numerous oligosaccharide synthesis.[43] The stereochemistry point of view in Ferrier rearrangement reveals that the formation of carbenium ion plays a crucial role on regio- and stereoselectivity. Indeed, the regioisomeric product depends upon the reaction condition and catalyst used in the medium. However, in case of acidic condition it offers stereoselective synthesis of 2,3-unsaturated-*O*-glycosides.

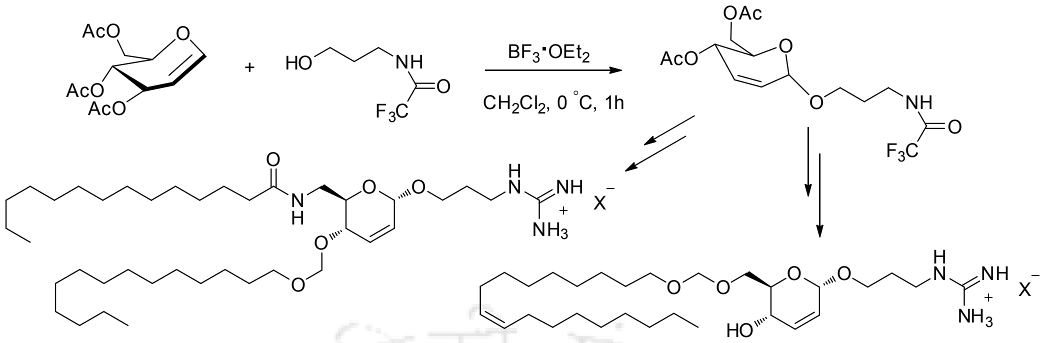
1.4a Synthetic Strategies and Development of Ferrier rearrangement on glucal

Ferrier reaction are extensively utilized for the construction of IRIDOID skeleton,[44] (+) Ratjadone[45] and partial synthesis of (-) Callystatin A[46] as depicted in Scheme 20.



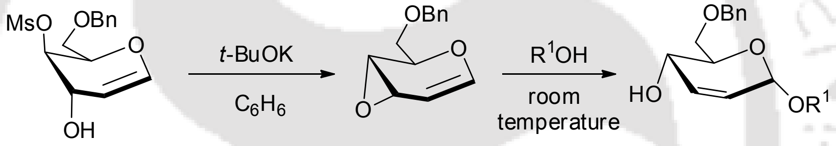
Scheme 20

Herscovici *et al.*[47] have described the synthesis of novel cationic lipids using 2,3-unsaturated-*O*-glycoside as key step which is shown in Scheme 21. The resulted amide/acetal units which reside on 2,3-unsaturated-*O*-glycoside at C6/C4 position direct to several mono- and bicatenar derivatives.



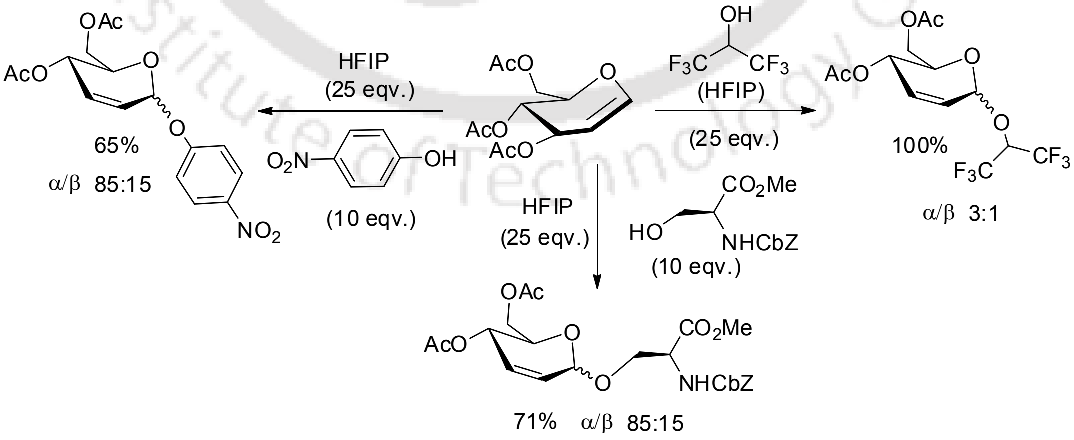
Scheme 21

Crotti *et al.*[48] demonstrated that hydroxy-mesylated glucal on reaction with potassium *tert*-butoxide led to unstable *in situ* generated vinyl oxirane, which further react with various alcohol at room temperature to furnish 4-hydroxy-2,3-unsaturated-α-*O*-glycoside which is depicted in Scheme 22.



Scheme 22

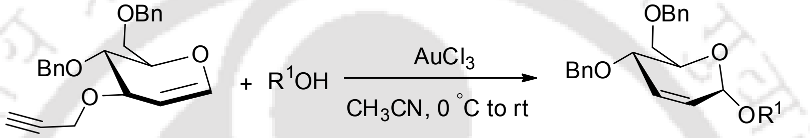
Bonnet-Delpon *et al.*[49] described that glucal on reaction with 25 equivalent of hexafluoro isopropanol (HFIP) at 80 °C afford hexafluoroisopropyl-2,3-unsaturated-α-*O*-glycoside as major one. However in presence of 10 equivalent of other alcohol such as



Scheme 23

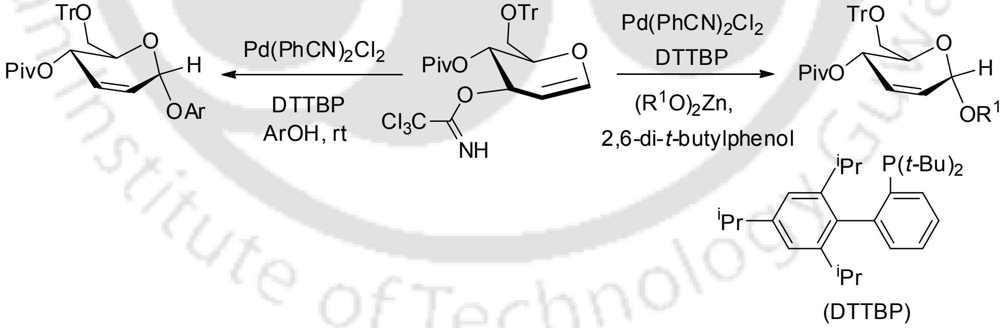
4-nitrophenol and *N*-protected serine alcohol which deliver 4-nitrophenyl-2,3-unsaturated-α-*O*-glycoside and *N*-protected serine-2,3-unsaturated-α-*O*-glycoside with 65% and 71% yield. It is important to note that in this case, hexafluoro isopropanol act as solvent-cum-abetting agent in the reaction medium as shown in Scheme 23.

Hotha *et al.*[50] developed a method wherein 4,6-di-*O*-benzyl-3-*O*-propargyl-ᴅ-glucal react with nucleophilic alcohol in presence of $AuCl_3$ as catalyst at 0 °C to room temperature to afford stereoselective 2,3-unsaturated-α-*O*-glycoside which is shown in Scheme 24.



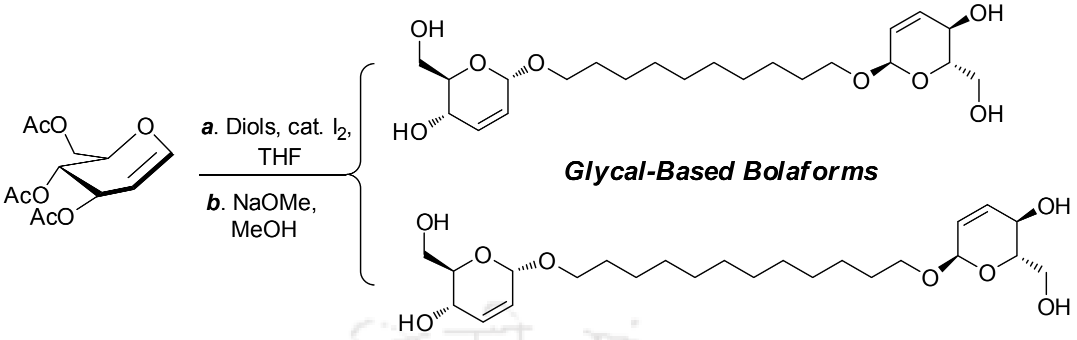
Scheme 24

Nguyen *et al.*[51] reported that glucal containing trichloroacetimidate group at the C-3 position react with zinc(II) alkoxide/ArOH using palladium(II)-biaryl phosphine as a catalyst at room temperature which offer 2,3-unsaturated-α-*O*-glycoside as shown in Scheme 25.



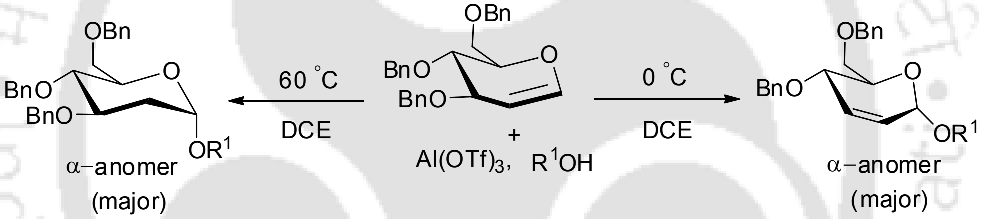
Scheme 25

Bozell *et al.*[52] demonstrated iodine catalyzed synthesis of *bis*-2,3-unsaturated-*O*-glycoside from 3,4,6-tri-*O*-acetyl-ᴅ-glucal and diols in THF at room temperature. The corresponding 2,3-unsaturated-*O*-glycoside were further deprotected to endure as glycal based bolaforms which is shown in Scheme 26.



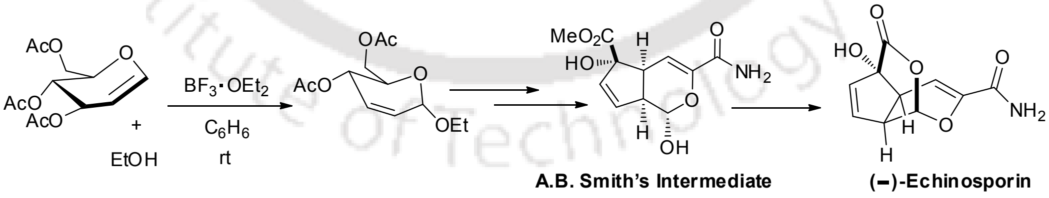
Scheme 26

Kinfe *et al.*[53] described the temperature mediated *O*-glycosides which revealed that 3,4,6-tri-*O*-benzyl-ᴅ-glucal react with alcohol in presence of Al(OTf)$_3$ at 0 °C in DCE leading to stereoselective 2,3-unsaturated-α-*O*-glycoside. However, at 60 °C it afforded 2-deoxy-*O*-glycoside of α-anomer which is depicted in Scheme 27.



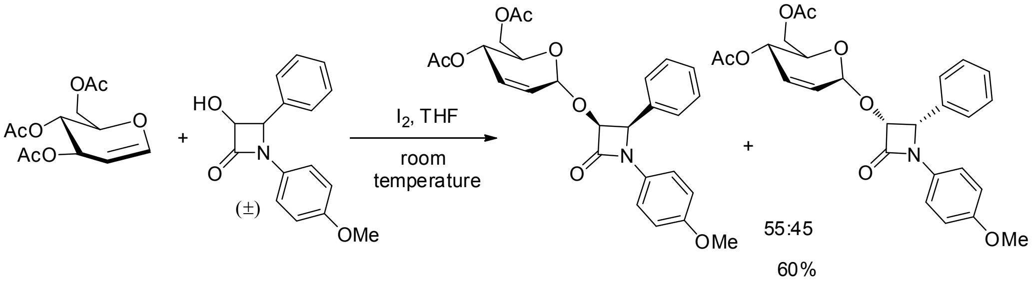
Scheme 27

Hale *et al.*[54] achieved the total synthesis of (-)-Echinosporin by utilizing 2,3-unsaturated-*O*-glycoside as a key step which is shown in Scheme 28.



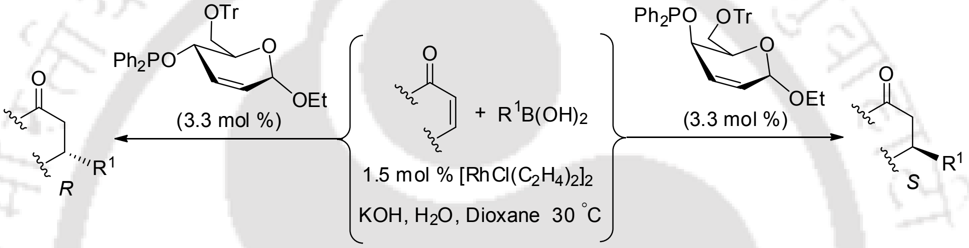
Scheme 28

Banik *et al.*[55] demonstrated the diastereomeric synthesis of 2,3-unsaturated-*O*-glycoside from 3,4,6-tri-*O*-acetyl-ᴅ-glucal and racemic *cis*-1-(*p*-anisyl)-3-hydroxy-4-phenyl-2-azetidinone in presence of iodine as catalyst in THF at room temperature which is depicted in Scheme 29.



Scheme 29

Boysen *et al.*[56] utilized the phosphinite hybrid of 2,3-unsaturated-*O*-glycoside as a novel diastereomeric ligand for asymmetric 1,4 addition as shown in Scheme 30.



Scheme 30

Other method have also been reported for the synthesis of 2,3-unsaturated-*O*-glycosides[41i] via Ferrier rearrangement using a variety of catalysts such as protic acids[57] or Lewis acids[41a-h] or metal triflates,[58] metal salts[59] and solid supported heterogeneous catalyst.[60] However, the drawbacks of these reported methods are: tedious work-up procedure, requirement of expensive catalysts, involvement of expensive microwave equipment, longer reaction time and harsh reaction conditions. Though, these methods are quite useful but still chemists are keen to look for milder reaction conditions with high stereoselectivity.

Overall literature survey reveals the importance of iodoglycosylation and Ferrier rearrangement on glucal, which constitute a major component in natural products and offer a diverse range of biomedical application. From this viewpoint, the challenging task to the synthetic chemists is to develop a new synthetic methodology for iodoglycosylation and Ferrier rearrangement, which are highly desirable. In the present thesis work a new methodology for the synthesis of 2-deoxy-2-iodo-*O*-glycoside and 2,3-unsaturated-*O*-glycosides has been developed, which are discussed in Chapter 2 and Chapter 3.

The methodology described in chapter 2 stems from the shadow of peroxovanadium chemistry. Vanadium haloperoxidase (isolated enzyme)[61] which catalyze the oxidation of halide[62] for the production of bromoorganics.[63] The reaction mechanism of this enzyme opens a new concept in synthetic platform.[64] Typically, vanadium peroxo complex formed in aqueous solution proceeds through interaction of vanadium metal with oxidant hydrogen peroxide.[65] Few years ago, Butler and her co-workers demonstrated the oxidation of bromide ion to bromonium ion using peroxovanadium complex and they extensively utilized the method for the bromination of organic substrates.[66] Taking cues from these reported method, the endeavor in the thesis work was to carry forward the novel concepts in carbohydrate chemistry.

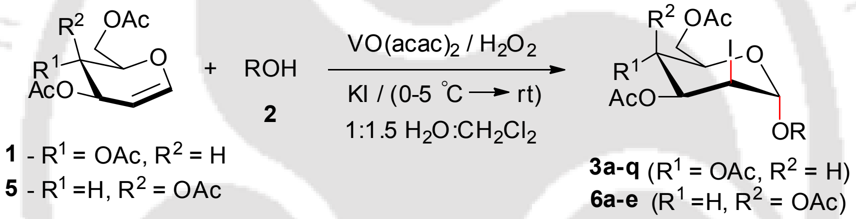
Chapter II

Aqueous Biphasic Mediated Stereoselective Synthesis of 2-deoxy-2-iodo-O-glycoside through in situ generated Iodonium ion Using Oxobis(acetylacetonato)vanadium

Results and Discussion

Results and Discussion

Under an aforementioned section of the Chapter I, we have discussed the 2-deoxy-2-iodo-*O*-glycoside structural unit importance and a traditional methods used for the synthesis of 2-deoxy-2-iodo-*O*-glycosidation. It is noteworthy to mention that glycosylation reactions are usually unfavourable in aqueous medium. We had recently developed an aqueous mediated efficient protocol for the cleavage of dithioacetal of sugars.[67] As a part of our ongoing research, we conceived that *in situ* generated iodonium ion in aqueous biphasic medium might be a straight forward methodology for the synthesis of 2-deoxy-2-iodo-*O*-glycoside derivatives. In this Chapter, we have demonstrated the *O*-glycosylation of glucal with alcohols using $VO(acac)_2/H_2O_2/KI$ at 0-5 °C to room temperature for the synthesis of 2-deoxy-2-iodo-*O*-glycoside derivatives which is shown in Scheme 31.



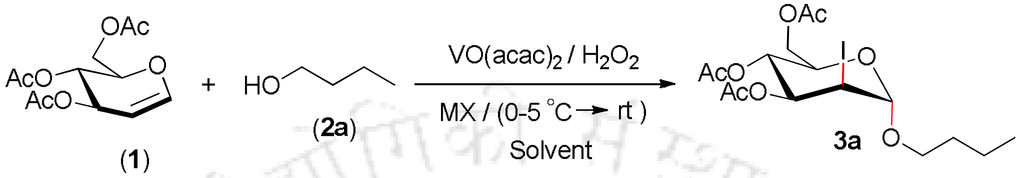
1 - R^1 = OAc, R^2 = H
5 - R^1 =H, R^2 = OAc

3a-q (R^1 = OAc, R^2 = H)
6a-e (R^1 =H, R^2 = OAc)

☐ **Scheme 31**. Synthesis of 2-deoxy-2-iodo-*O*-glycosides

At the beginning of our study, a model reaction was conducted with 3,4,6-tri-*O*-acetyl-D-glucal (**1**) and *n*-butanol (**2a**) to find out the optimal reaction conditions and the obtained results are summarized in Table 1. In absence of the catalyst, only with H_2O_2/MX the reaction did not take place under similar reaction condition (Table 1, entry 1 & 4). Moreover, different molar ratio of the catalyst $VO(acac)_2$, oxidizer H_2O_2, metal halide MX were scrutinized and the best result were obtained with the molar ratio of 0.2/2.14/1.5 in terms of yield and selectivity (Table 1, entry 7). As the molar ratio of the oxidant H_2O_2 increased, there was an increase in the yield (Table 1, entry 6 & 7). We also observe that excess loading of the catalyst $VO(acac)_2$ decreases the yield and selectivity (Table 1, entry 8). It is noteworthy that among the metal halide MX source, KI was found to be the most suitable for the synthesis of 2-deoxy-2-iodo-*O*-glycoside. It may be due to the formation of stable KI_3 in the reaction medium. The various solvent screening (Table 1, entry 7 & 9-12) shows that H_2O/CH_2Cl_2 was found to be the best solvent for the synthesis of 2-deoxy-2-iodo-*O*-glycoside. Furthermore, the isolated product **3a** was characterized by ^{1}H NMR which shows the peak at 5.10 as broad singlet for H1, doublet of doublet for H2 at 4.46 (*J* = 4.4, 1.2 Hz) and the C1-alkoxy, C2-iodo in the ^{13}C NMR which appears at 101.4, 29.9 ppm respectively.

Table 1. Optimization of the reaction conditions [a]

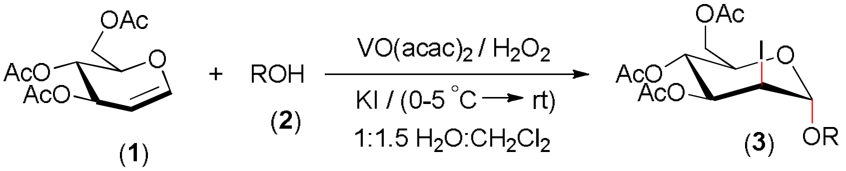


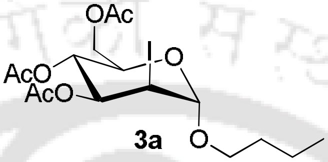
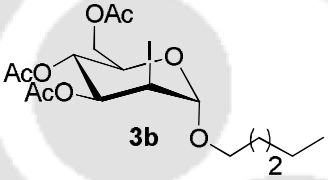
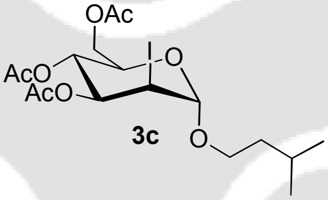
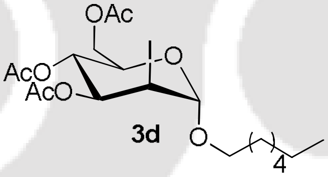
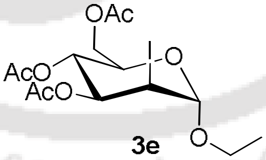
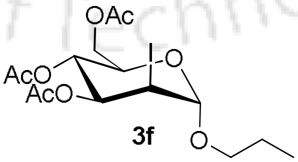
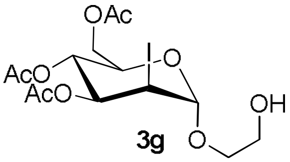
Entry	VO(acac)$_2$ mol % / 30 % H$_2$O$_2$ mL	Solvent	MX (mmol)	Time (h)	Yield (%)[b]	α : β[c]
1	-/0.12	H_2O/CH_2Cl_2	NaI (0.5)	24	NR	-
2	10/0.06	H_2O/ CH_2Cl_2	NaI (0.75)	14	<10	2:1
3	15/0.06	H_2O/CH_2Cl_2	NaI (0.75)	12	<20	2:1
4	-/0.12	H_2O/CH_2Cl_2	KI (0.75)	34	NR	-
5	10/0.06	H_2O/CH_2Cl_2	KI (0.5)	12	42	3:1
6	15/0.06	H_2O/CH_2Cl_2	KI (0.5)	10	45	4:1
7	**20/0.12**	$\mathbf{H_2O/CH_2Cl_2}$	**KI (0.75)**	**3**	**75**	**12:1**
8	25/0.12	H_2O/CH_2Cl_2	KI (0.75)	4	70	9:1
9	20/0.12	H_2O/CH_3CN	KI (0.75)	3.5	65	7:1
10	20/0.12	H_2O/EtOAc	KI (0.75)	5	68	5:1
11	20/0.12	H_2O/Acetone	KI (0.75)	4	62	6:1
12	20/0.12	H_2O/THF	KI (0.75)	4.5	58	4:1

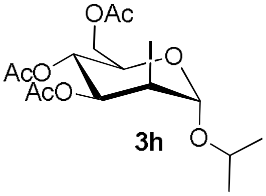
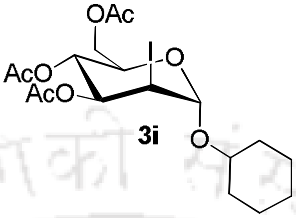
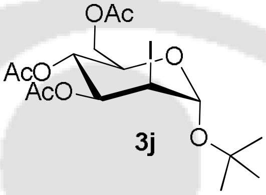
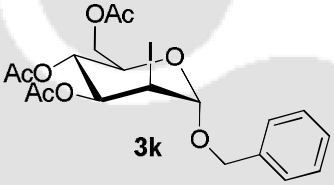
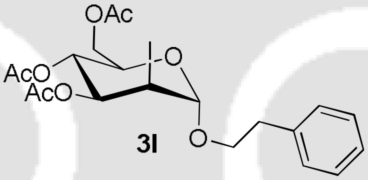
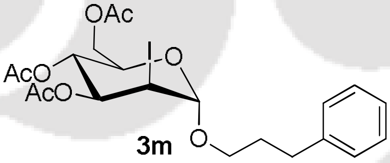
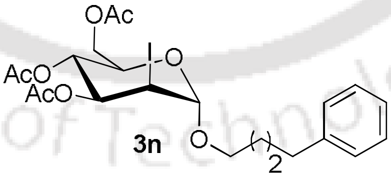
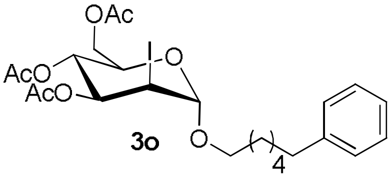
[a] The reactions were performed using 0.5 mmol scale of 3,4,6-tri-*O*-acetyl-D-glucal (**1**) and *n*-butanol (**2a**). [b] Isolated yield. [c] The ratio of α:β was determined by anomeric proton integration from ^{1}H NMR spectra.

We have performed the reactions with a variety of alcohols (**2b-f**) and 3,4,6-tri-*O*-acetyl-D-glucal (**1**) under similar reaction conditions which readily afforded the product (**3b-f**) with moderate to good yields (Table 2, entries 2-6). In the case of ethylene glycol (**2g**), the yield was only 52% (Table 2, entry 7). Encouraged by these results, the reaction was carried out using secondary and tertiary alcohols such as isopropanol (**2h**), cyclohexanol (**2i**) and *tert*-butanol (**2j**) with 3,4,6-tri-*O*-acetyl-D-glucal (**1**) which gave the desired product (**3h-j**) of 2-deoxy-2-iodo-*O*-glycoside in 62-88% yield (Table 2, entries 8-10). To examine the compatibility of the present protocol, we have conducted the reaction with phenyl alkyl alcohols such as benzyl alcohol (**2k**), 2-phenylethanol (**2l**), 3-phenylpropol (**2m**), 4-phenylbutanol (**2n**) and 6-phenylhexanol (**2o**) with 3,4,6-tri-*O*-acetyl-D-glucal (**1**) under identical reaction condition which gave the corresponding product (**3k-o**) in 40-72% yield (Table 2, entries 11-15).

Table 2. Iodoglycosidation of 3,4,6-tri-*O*-acetyl-D-glucal[a]



S.No	Alcohol (**2**)	Product (**3**)	Time (h)	Yield (%)[b]	α:β[c]
01	*n*-butanol **2a**	 **3a**	2.5	87	11:1
02	Amyl alcohol **2b**	 **3b**	3.5	82	12:1
03	Isoamylalcohol **2c**	 **3c**	10	63	α
04	Heptan-1-ol **2d**	 **3d**	4	72	14:1
05	Ethanol **2e**	 **3e**	3.5	88	12:1
06	*n*-propanol **2f**	 **3f**	3	85	10:1
07	Ethyleneglycol **2g**	 **3g**	12	52	8:1

08	Isopropanol **2h**	 **3h**	5	82	11:1
09	Cyclohexanol **2i**	 **3i**	3.5	88	α
10	*tert*-butanol **2j**	 **3j**	4.5	62	12:1
11	Benzyl alcohol **2k**	 **3k**	8	72	12:1
12	2-Phenyl ethanol **2l**	 **3l**	8.5	55	10 :1
13	3-Phenyl prop-1-ol **2m**	 **3m**	6.5	42	5:1
14	4-Phenyl butan-1-ol **2n**	 **3n**	7	62	7:1
15	6-Phenyl hexan-1-ol **2o**	 **3o**	8	40	4:1

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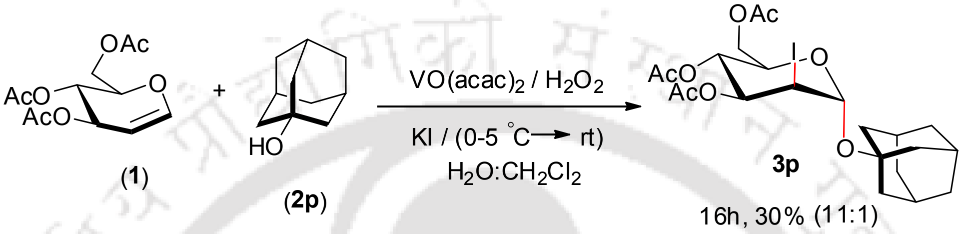
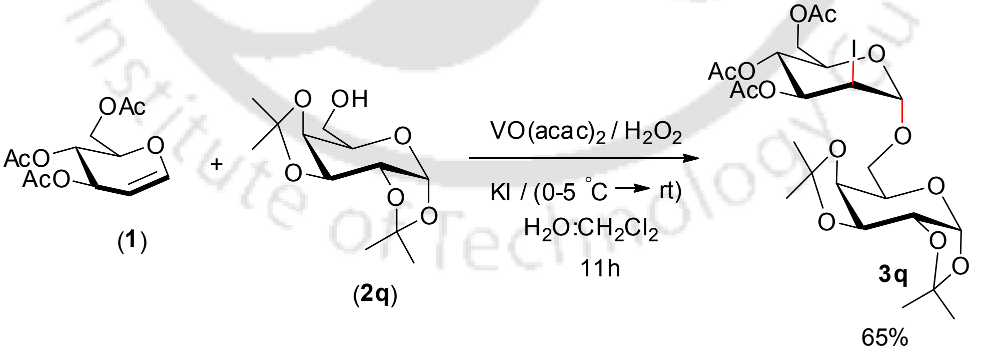
[a] All the reactions were performed using VO(acac)$_2$, H_2O_2, KI in H_2O:CH_2Cl_2 with 3,4,6-tri-*O*-acetyl-D-glucal (0.5 mmol) and alcohol (0.5 mmol). [b] Isolated yield. [c] The ratio α:β was determined by anomeric proton integration from ^{1}H NMR.

The successfully achieved results of 2-deoxy-2-iodo-*O*-glycoside derivative **3** α:β ratio, reaction time and yield are summarized in Table 2. All the isolated products were fully characterized by IR, NMR and elemental analysis. Moreover, the present protocol was further verified on reaction with sterically hindered tertiary alcohol such as adamantol (**2p**) under identical reaction condition and the isolated product **3p** was obtained with 30% yield which is shown in Scheme 32.



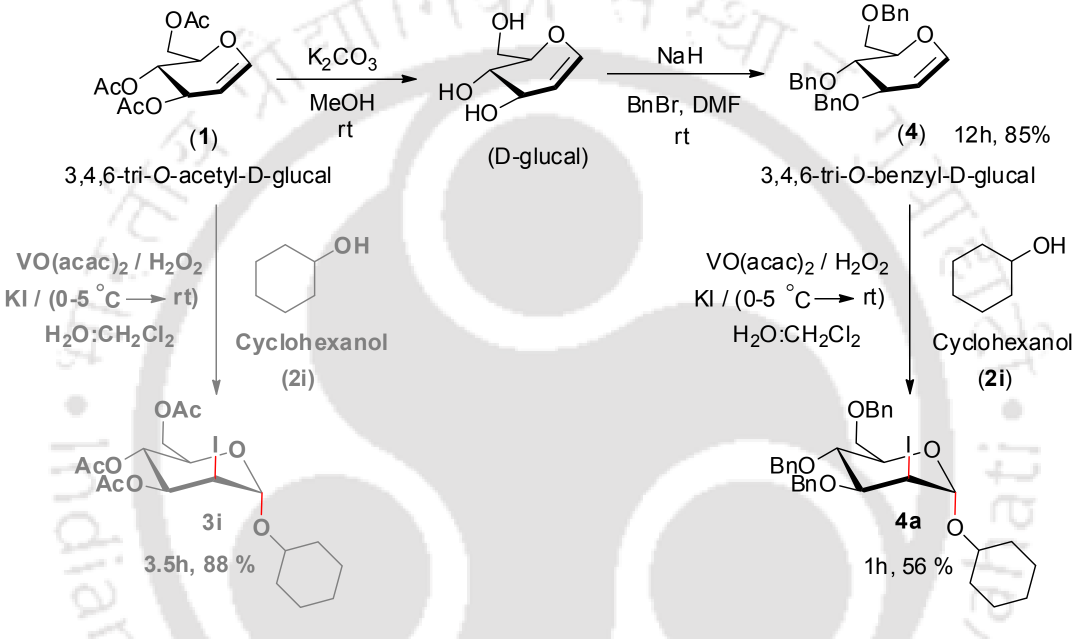
Scheme 32. Synthesis of adamantyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-iodo-*O*-glycoside

Furthermore on reaction with glucal (**1**), glycosyl acceptor 1,2,3,4-di-*O*-isopropylidene-ᴅ-galactopyranoside (**2q**) under similar reaction conditions and the time taken for the completion of the reaction were 11h and the corresponding product **3q** of α-anomer were obtained with 65% yield as shown in Scheme 33. It is thus clear that present protocol works well with acid sensitive glycosyl acceptor. In addition to that, Lafont *et al.* demonstrated the synthesis of Iodo-disaccharide **3q** with two consequent steps under drastic experimental conditions[32] which attain the overall yield with only 58.3% respectively.



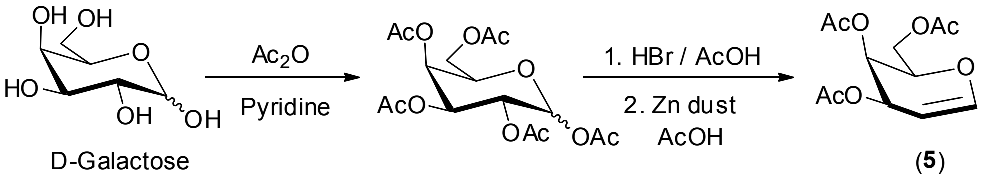
Scheme 33. Stereoselective synthesis of 2-deoxy-2-iodo-disaccharide

Next, we wanted to study whether different protecting group on the glucal moiety play an important role in reactivity and selectivity.[29,35] For this study, we have synthesized 3,4,6-tri-*O*-benzyl-ᴅ-glucal (**4**) from 3,4,6-tri-*O*-acetyl-ᴅ-glucal (**1**) via two steps, *i.e.* deprotection with potassium carbonate in methanol followed by benzylation using sodium hydride.[68] The reaction was conducted with 3,4,6-tri-*O*-benzyl-D-glucal (**4**) with cyclohexanol (**2i**) under similar experimental conditions which gave the required product **4a** in 56% yield as shown in Scheme 34. When we compared the output of the result with **3i**, the reaction time was shorter and the yield was lesser. From this, we may conclude that in our present protocol the reactivity of benzylated-D-glucal (**4**) is more as compare to acetylated-D-glucal (**1**). However, in case of stereoselectivity both **3i** & **4a** prefer to form only α anomer.



Scheme 34. Synthesis of cyclohexyl 3,4,6-tri-*O*-benzyl-2-deoxy-2-iodo-*O*-glycoside

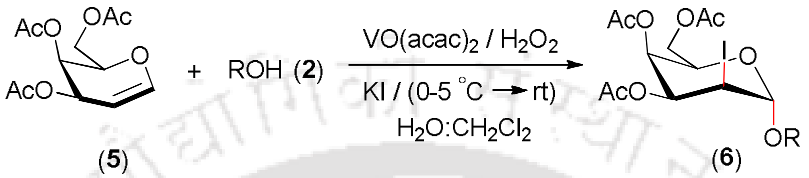
We have prepared 3,4,6-tri-*O*-acetyl-D-galactal (**5**) from D-galactose via three steps[69] which is shown in Scheme 35. The obtained galactal (**5**) on reaction with isopropyl alcohol (**2h**) under analogous reaction conditions gave the desired product **6a** in 52% yield.

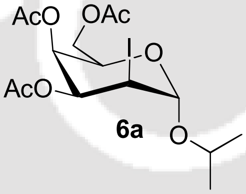
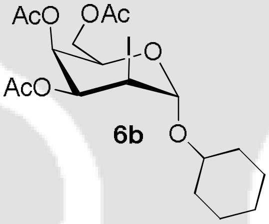
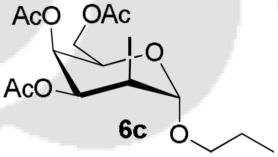
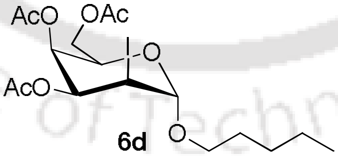
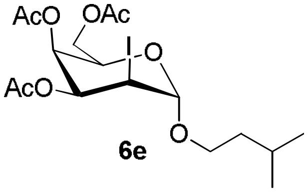


Scheme 35. Synthesis of 3,4,6-tri-*O*-acetyl-D-galactal

Likewise, a variety of alcohols such as cyclohexanol (**2i**), *n*-propanol (**2f**), amyl alcohol (**2b**) and isoamyl alcohol (**2c**) underwent reactions with 3,4,6-tri-*O*-acetyl-D-galactal (**5**) under similar reaction condition which gave the corresponding products (**6b-e**) in 55-82% yield which is depicted in Table 3. Furthermore, the structure of the compound **6a** was confirmed through single X-ray diffraction data as shown in Figure 2a.

Table 3. Iodo-galactosidation of 3,4,6-tri-*O*-acetyl-ᴅ-galactal[a]



S.No	ROH (**2**)	Product (**6**)	Time (h)	Yield (%)[b]	α:β[c]
01	Isopropanol **2h**		12	52	α
02	Cyclohexanol **2i**		2	77	α
03	*n*-propanol **2f**		16	73	α
04	Amyl alcohol **2b**		15	55	12:1
05	Isoamyl alcohol **2c**		14	82	14:1

[a] All the reactions were performed using 3,4,6-tri-*O*-acetyl-ᴅ-galactal (0.5 mmol) and alcohol (0.5 mmol) in $H_2O:CH_2Cl_2$. [b] Isolated yield. [c] The ratio of α:β was determined from ^1H NMR.

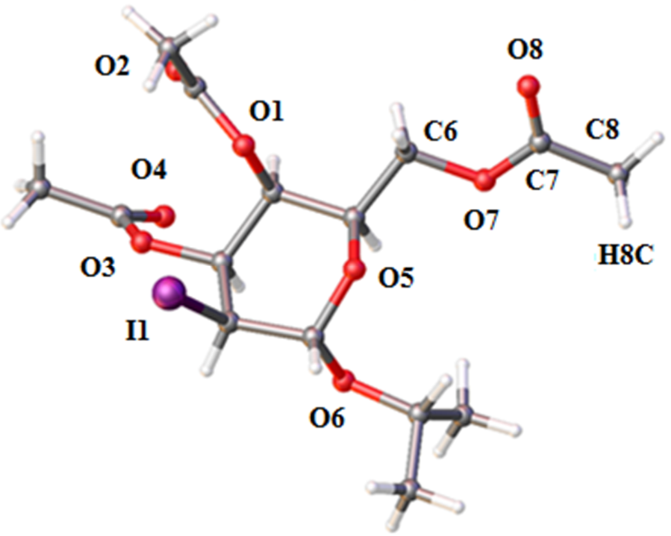


Figure 2a. X-ray crystal structure of **6a**

Crystal engineering perspectives in organic molecules have received particular attention in recent years.[70] However, the engineered structure of the crystal network mainly depend upon the weak interactions among the molecule. In addition, the molecule **6a** crystallized from chloroform and appeared as orthorhombic crystal system with $P2_12_12_1$ space group. Each unit cell contain four molecules of **6a** and the crystal packing revealed

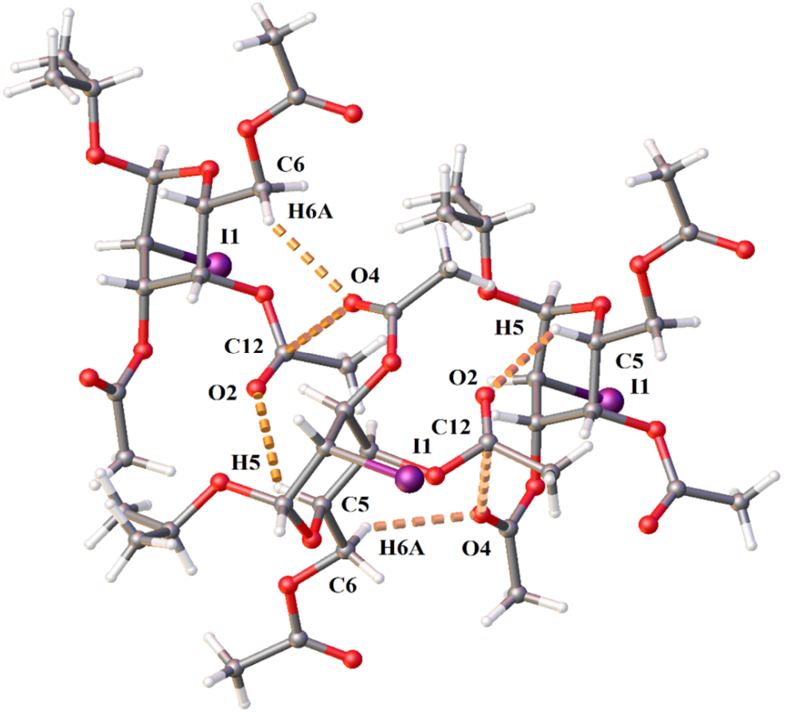


Figure 2b. Interactions of O4…H6A, O4…C12 and C5H5…O2 in **6a**

that an intermolecular interaction with O4….H6A, O4…C12 and H5…O2 exhibit an interesting fused bicyclo seven and eight membered supramolecular assembly which is shown in Figure 2b. On the other hand O5…H8C interactions in **6a** forms a fascinating zigzag structure as depicted in Figure 2c.

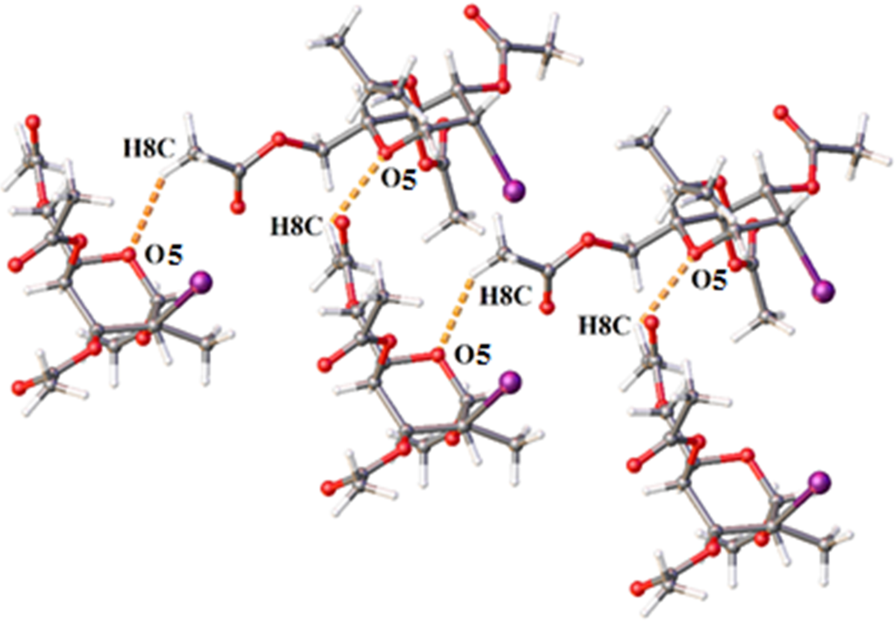
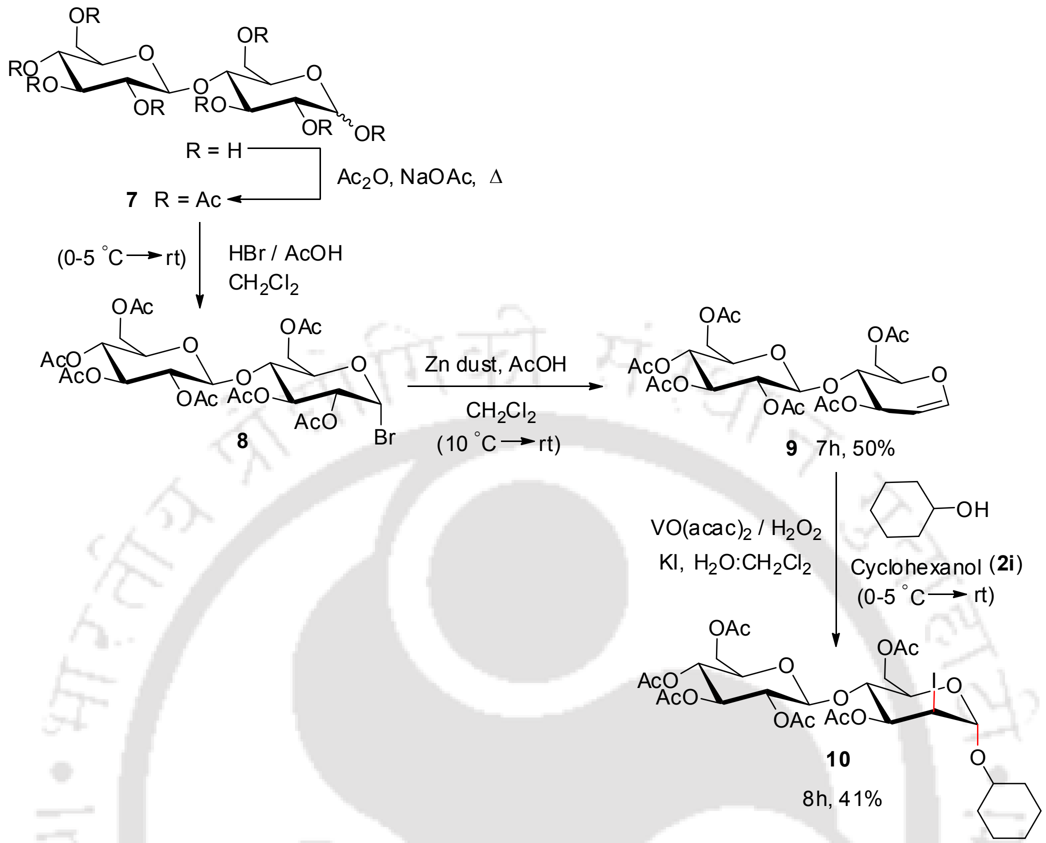


Figure 2c. Interactions of O5…H8C in **6a**

The framework of iodo-disaccharide unit might be useful for biomedical application in near future. We prefer to investigate our synthetic protocol on disaccharide unit assembly. At first hexa-*O*-acetyl-cellobial **9** was synthesized via three steps i.e., acetylation,[71a] anomeric α-bromination followed by reduction with zinc dust in acetic acid.[69] Subsequently, the obtained disaccharide glucal **9** on reaction with cyclohexanol (**2i**) under identical reaction condition formed only α anomer of 2-deoxy-2-iododisaccharide **10** in 41% yield as shown in Scheme 36. In addition, the structure of compound **10** was confirmed through single x-ray crystal data which is depicted in Figure 3a. The molecular packing of **10** exists as layered structure which is represented in Figure 3b. Moreover, O6...I1 interaction in **10** revealed significant supramolecular architecture as shown in Figure 3c.

Our subsequent endeavour was to explore the present protocol on lactose unit. Initial reaction was performed with lactose **11**, acetic anhydride and sodium acetate under reflux condition to afford lactose octaacetate **12**.[71a]



Scheme 36. Iodo-glycosidation of Hexa-*O*-acetyl-cellobial

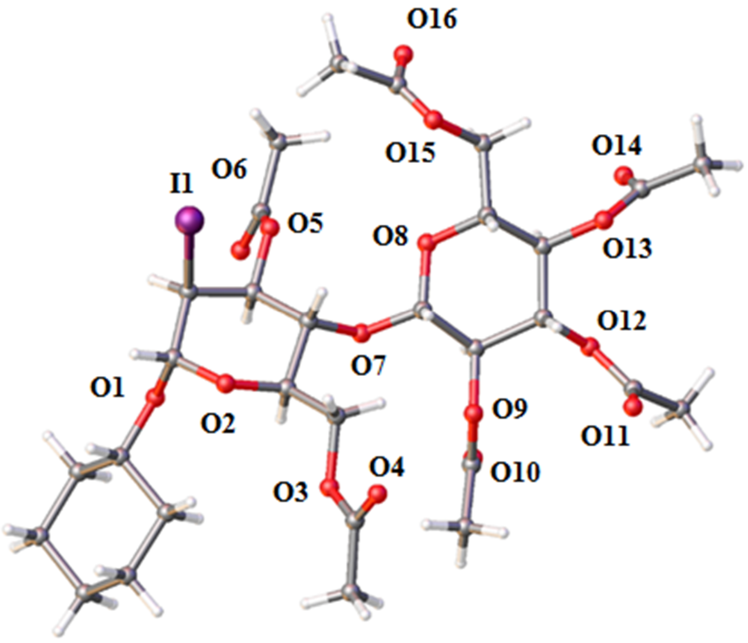


Figure 3a. X-ray crystal structure of **10**

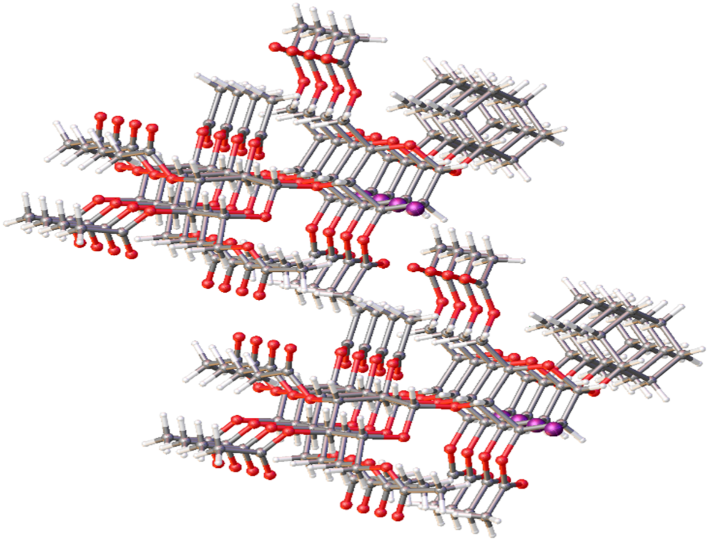


Figure 3b. Layered structure of **10**

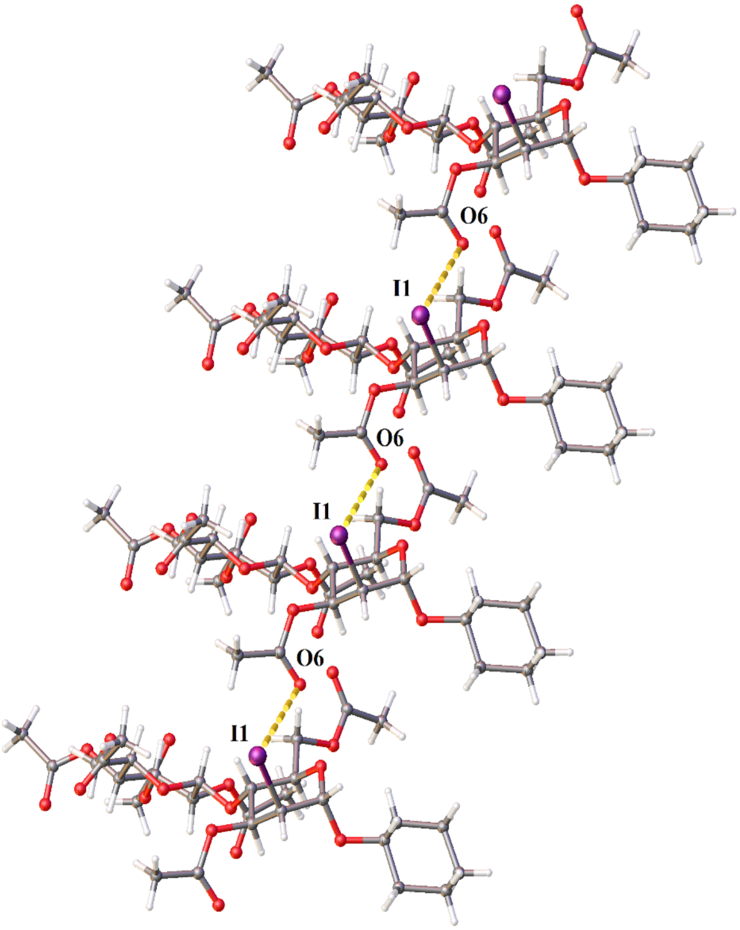
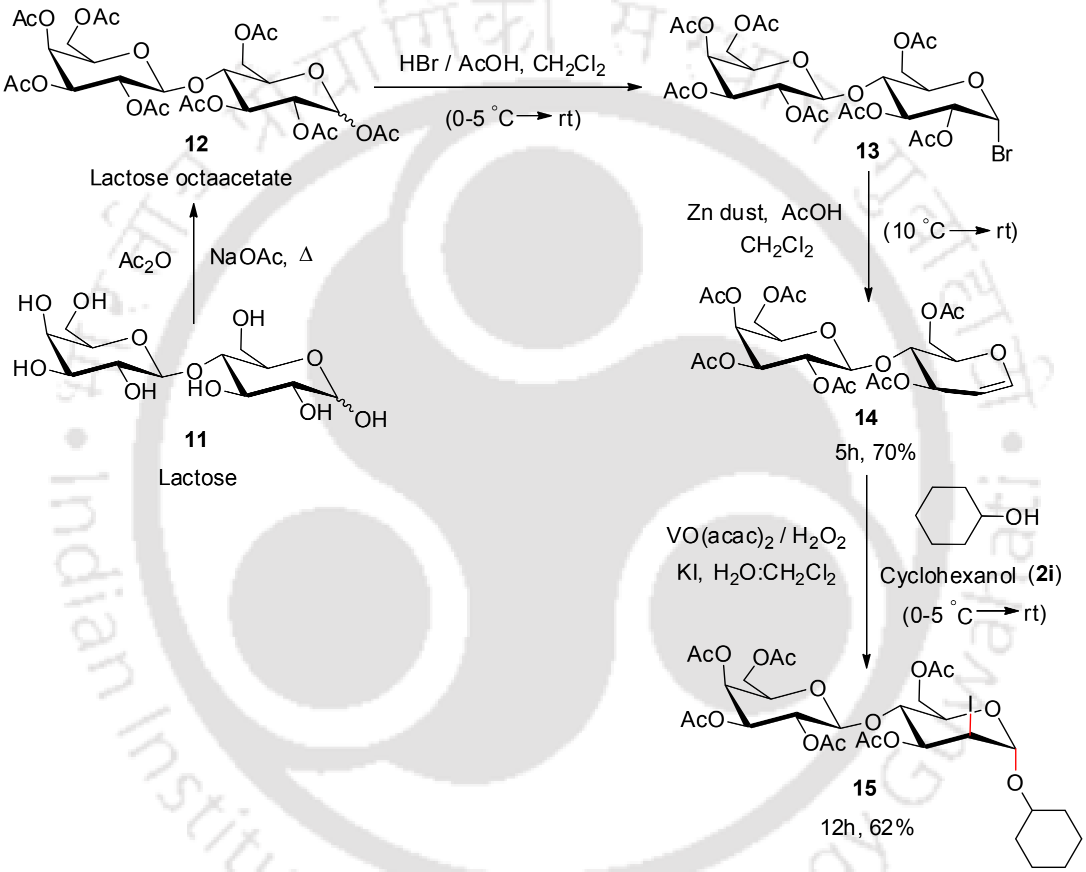


Figure 3c. O6...I1 interaction of **10**

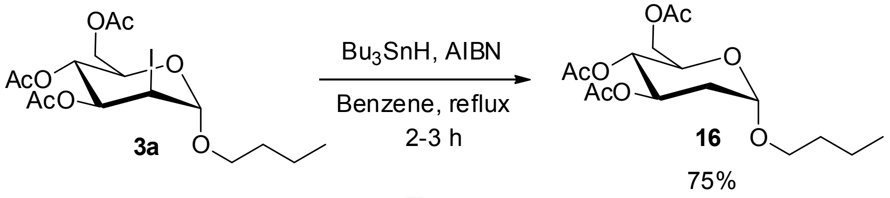
Later on, the compound **12** reacted with HBr in acetic acid and gave the desired product of acetobromo-α-D-lactose **13**. Subsequently, on reduction with Zn dust/acetic acid, hexa-*O*-acetyl-lactobial **14**[71b] formed with 70% yield. The obtained lactobial **14** were treated with cyclohexanol (**2i**) in presence of $VO(acac)_2/H_2O_2$ and KI in $H_2O:CH_2Cl_2$ under similar reaction condition which provide the required product **15** in 62% yield with only α anomer which is shown in Scheme 37.



Scheme 37. Iodo-glycosidation of Hexa-*O*-acetyl-lactobial

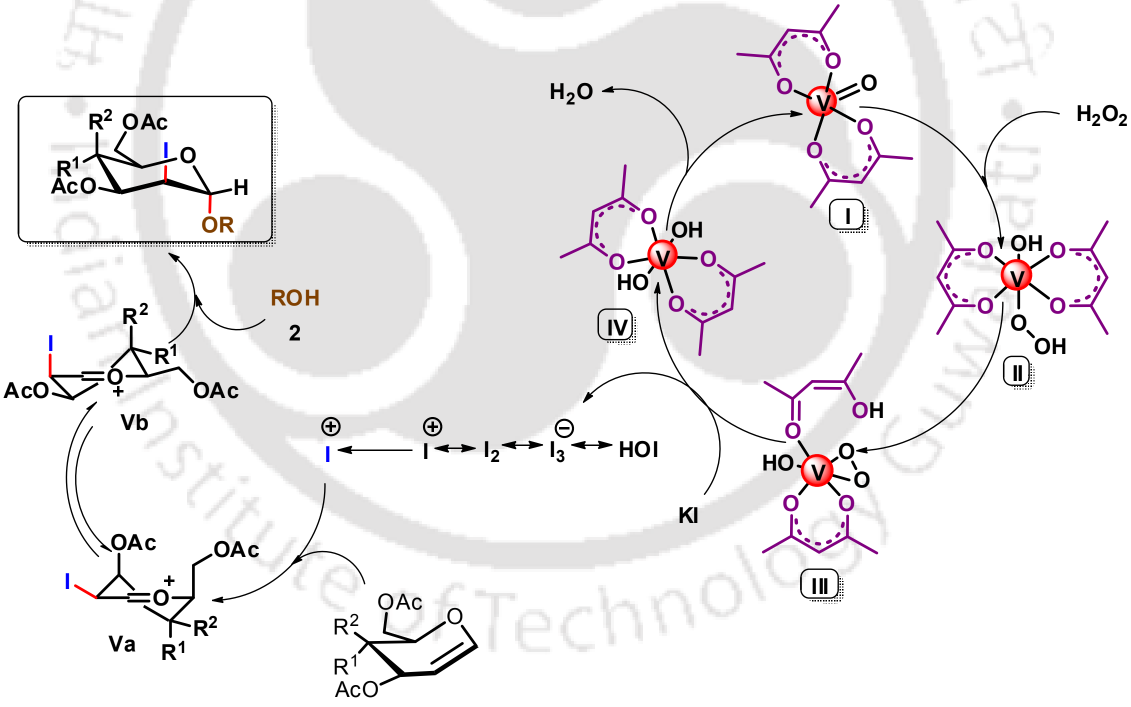
Generally 2-deoxy-*O*-glycoside was synthesized from 2-deoxy-2-iodo-*O*-glycoside through reductive deiodination. From this outlook, we have conducted a reaction with butyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-iodo-*O*-glycoside **3a**, tributyltin hydride in presence of radical initiator azobis isobutyronitrile in benzene under reflux condition which gave the corresponding product **16** in 75% yield as shown in Scheme 38.

The formation of the product 2-deoxy-2-iodo-*O*-glycoside is described as follows, Initially $VO(acac)_2$ **I** reacts with H_2O_2 to form **II** which undergoes further rearrangement to form vanadium mono peroxocomplex **III**. The incoming halide ion I^- from potassium iodide, which will oxidize from vanadium mono peroxocomplex **III** to form iodonium ion (which might exist as $I_3^- \leftrightarrow I_2 \leftrightarrow$ HOI in the solution).



Scheme 38. Synthesis of butyl 3,4,6-tri-*O*-acetyl-2-deoxy-ᴅ-glycopyranoside

Moreover, the liberated iodonium ion I^+ reacts with glucal to forms the two possible conformers of **Va** and **Vb**. In terms of stability and its reactivity toward the incoming nucleophile it favours **Vb** for further attack with nucleophilic alcohol **2** to form highly stereoselective α anomer of 2-deoxy-2-iodo-*O*-glycoside as a predominant one as shown in Scheme 39.



R¹ = OAc, R² = H / R¹ = H, R² = OAc / R¹ = β-Glucosyl, β-Galactosyl, R² = H

Scheme 39. Plausible mechanism for the formation of 2-deoxy-2-iodo-*O*-glycoside

In summary, we have devised a greener protocol for the synthesis of 2-deoxy-2-iodo-*O*-glycoside using VO(acac)$_2$, H_2O_2 and KI in aqueous based biphasic medium. The main features of the present protocol are simple, eco-friendly, mild reaction condition, highly stereoselective and compatible with a wide range of substrate. Moreover, the present protocol is a straight forward methodology for the synthesis of 2-deoxy-2-iodo-*O*-glycosides and it was further explored for the synthesis of 2-deoxy-*O*-glycoside. However, the chemical synthesis of *O*-glycosylated product needs anhydrous reaction conditions. But the present protocol will proceed through aqueous biphasic medium. To the best of our knowledge, this is the first reported method of *O*-glycosylation in aqueous biphasic medium for the synthesis of 2-deoxy-2-iodo-*O*-glycosides. In addition to that, the molecule **6a** and **10** exhibit fascinating supramolecular scaffolds.

Experimental Section

Chapter II

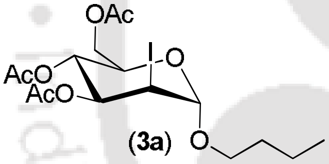
Aqueous Biphasic Mediated Stereoselective Synthesis of 2-deoxy-2-iodo-O-glycoside through in situ generated Iodonium ion Using Oxobis (acetylacetonato)vanadium

Experimental

General procedure for the synthesis of 2-deoxy-2-iodo-O-glycosides

A mixture of VO(acac)$_2$ (0.1 mmol, 0.026 g) in 1 mL water followed by 30% hydrogen peroxide (1.07 mmol, 0.12 mL) was added at 0-5 °C and allow to stir till pale yellow color persisted. Then KI (0.75 mmol, 0.124 g)/1 mL H$_2$O was added to the reaction medium and a dark brown color appeared. Subsequently, glucal (0.5 mmol)/1.5 mL CH$_2$Cl$_2$ and alcohol (0.5 mmol)/1.5 mL CH$_2$Cl$_2$ was added and allowed to stir for appropriate time as shown in Table 2. Later on, the reaction mixture was extracted with DCM (2 x 25 mL) and it was washed with 10% sodium thiosulphate and dried over sodium sulfate and concentrate under reduced pressure to obtain the crude residue, which was further subjected to silica gel column chromatography to obtain the pure product of 2-deoxy-2-iodo-*O*-glycoside.

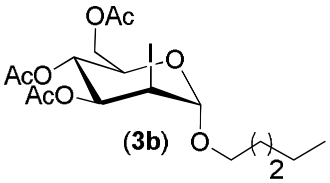
*Butyl 3,4,6-tri-O-acetyl-2-deoxy-2-iodo-D-mannopyranoside **(3a)***



(3a)

$[\alpha]_D^{25}$ +12° (*c* 0.106, CH$_2$Cl$_2$); **IR** (KBr) 2959, 2929, 2867, 1750, 1367, 1227, 1119, 1042 cm^{-1}; ^{1}**H NMR** (400 MHz, CDCl$_3$): δ 5.30 (t, *J* = 9.6 Hz, 1H), 5.10 (bs, 1H), 4.57 (dd, *J* = 9.2 Hz, *J* = 4.0 Hz, 1H), 4.46 (dd, *J* = 4.4 Hz, *J* = 1.2 Hz, 1H), 4.16 (dd, *J* = 12.0 Hz, *J* = 4.8 Hz, 1H), 4.08 (dd, *J* = 12.0 Hz, *J* = 2.0 Hz, 1H), 3.95 (ddd, *J* = 10.0 Hz, *J* = 4.8 Hz, *J* = 2.4 Hz, 1H), 3.61 (dt, *J* = 10.0 Hz, *J* = 6.4 Hz, 1H), 3.40 (dt, *J* = 9.6 Hz, *J* = 6.4 Hz, 1H), 2.05 (s, 3H), 2.02 (s, 3H), 1.99 (s, 3H), 1.54-1.50 (m, 2H), 1.35-1.29 (m, 2H), 0.87 (t, *J* = 7.2 Hz, 3H); ^{13}**C NMR** (100 MHz, CDCl$_3$): δ 170.8, 170.0, 169.6, 101.4, 69.3, 69.2, 68.5, 67.7, 62.4, 31.5, 29.9, 21.0, 20.8, 20.7, 19.4, 13.9. **Anal. Calcd** for C$_{16}$H$_{25}$IO$_8$ (472.26): C, 40.69; H, 5.34. Found: C, 40.54; H, 5.22%.

*Pentyl 3,4,6-tri-O-acetyl-2-deoxy-2-iodo-D-mannopyranoside **(3b)***

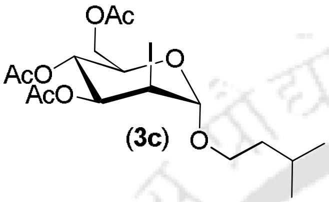


(3b)

$[\alpha]_D^{25}$ +9° (*c* 0.042, CH$_2$Cl$_2$); **IR** (KBr) 2921, 2850, 1736, 1654, 1438, 1365, 1221, 1116, 1042, 966 cm^{-1}; ^{1}**H NMR** (400 MHz, CDCl$_3$): δ 5.36 (t, *J* = 9.6 Hz, 1H), 5.16 (bs, 1H), 4.64 (dd, *J* = 9.6 Hz, *J* = 4.4 Hz, 1H), 4.53 (dd, *J* = 4.4 Hz, *J* = 1.2 Hz, 1H), 4.22 (dd, *J* = 12.0 Hz, *J* = 4.8 Hz, 1H), 4.14 (dd, *J* = 12.0 Hz, *J* = 2.4 Hz, 1H), 4.01 (ddd, *J* = 10.0 Hz, *J* = 4.8 Hz, *J* = 2.4 Hz, 1H), 3.66 (dt, *J* = 9.6 Hz, *J*

= 6.8 Hz, 1H), 3.45 (dt, *J* = 9.6 Hz, *J* = 6.4 Hz, 1H), 2.11 (s, 3H), 2.08 (s, 3H), 2.05 (s, 3H), 1.62-1.58 (m, 3H), 1.34-1.31 (m, 3H), 0.91 (t, *J* = 6.8 Hz, 3H);^{13}**C NMR** (100 MHz, $CDCl_3$): δ 170.9, 170.0, 169.7, 101.5, 69.3, 68.9, 67.8, 62.5, 30.0, 29.2, 28.3, 22.5, 21.1, 20.9, 20.8, 14.1. **Anal. Calcd** for $C_{17}H_{27}IO_8$ (486.29): C, 41.99; H, 5.60. Found: C, 41.87; H, 5.46%.

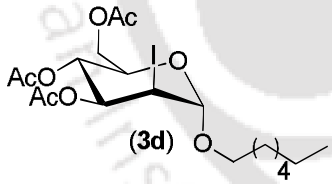
*Isopentyl 3,4,6-tri-O-acetyl-2-deoxy-2-iodo-D-mannopyranoside (**3c**)*



(3c)

$[\alpha]_D^{25}$ +13° (*c* 0.066, CH_2Cl_2); **IR** (KBr) 2957, 2924, 1745, 1466, 1367, 1225, 1118, 1050 cm^{-1}; ^{1}**H NMR** (600 MHz, $CDCl_3$): δ 5.35 (t, *J* = 9.6 Hz, 1H), 5.15 (bs, 1H), 4.63 (dd, *J* = 9.0 Hz, *J* = 4.2 Hz, 1H), 4.51 (dd, *J* = 4.2 Hz, *J* = 1.2 Hz, 1H), 4.21 (dd, *J* = 12.0 Hz, *J* = 4.8 Hz, 1H), 4.14 (dd, *J* = 12.0 Hz, *J* = 1.8 Hz, 1H), 4.00 (ddd, *J* = 9.6 Hz, *J* = 4.8 Hz, *J* = 1.8 Hz, 1H), 3.70 (dt, *J* = 10.2 Hz, *J* = 7.2 Hz, 1H), 3.48 (dt, *J* = 9.6 Hz, *J* = 7.2 Hz, 1H), 2.10 (s, 3H), 2.07 (s, 3H), 2.05 (s, 3H), 1.70-1.67 (m, 1H), 1.51-1.46 (m, 2H), 0.91 (d, *J* = 2.4 Hz, 3H), 0.90 (d, *J* = 2.4 Hz, 3H); ^{13}**C NMR** (100 MHz, $CDCl_3$): δ 170.8, 170.0, 169.7, 101.4, 69.2, 67.7, 67.2, 62.4, 38.2, 29.9, 25.0, 22.7, 22.5, 21.1, 20.9, 20.8. **Anal. Calcd** for $C_{17}H_{27}IO_8$ (486.29): C, 41.99; H, 5.60. Found: C, 41.89; H, 5.48%.

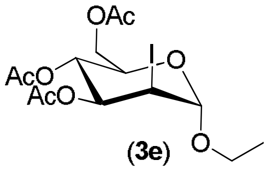
*Heptyl 3,4,6-tri-O-acetyl-2-deoxy-2-iodo-D-mannopyranoside (**3d**)*



(3d)

$[\alpha]_D^{25}$ +11° (*c* 0.082, CH_2Cl_2); **IR** (KBr) 2928, 2842, 1752, 1585, 1368, 1226, 1127, 1044 cm^{-1}; ^{1}**H NMR** (400 MHz, $CDCl_3$): δ 5.34 (t, *J* = 9.6 Hz, 1H), 5.14 (bs, 1H), 4.62 (dd, *J* = 9.6 Hz, *J* = 4.4 Hz, 1H), 4.50 (dd, *J* = 4.4 Hz, *J* = 1.2 Hz, 1H), 4.20 (dd, *J* = 12.0 Hz, *J* = 4.8 Hz, 1H), 4.12 (dd, *J* = 12.0 Hz, *J* = 2.0 Hz, 1H), 3.99 (ddd, *J* = 10.0 Hz, *J* = 4.8 Hz, *J* = 2.4 Hz, 1H), 3.63 (dt, *J* = 9.6 Hz, *J* = 6.8 Hz, 1H), 3.43 (dt, *J* = 9.6 Hz, *J* = 6.4 Hz, 1H), 2.09 (s, 3H), 2.06 (s, 3H), 2.03 (s, 3H), 1.60-1.56 (m, 2H), 1.29-1.23 (m, 8H), 0.87 (t, *J* = 6.0 Hz, 3H);^{13}**C NMR** (100 MHz, $CDCl_3$): δ 170.9, 170.0, 169.7, 101.4, 69.3, 69.2, 68.9, 67.8, 62.4, 31.9, 29.9, 29.5, 29.1, 26.2, 22.7, 21.1, 20.9, 20.8, 14.2. **Anal. Calcd** for $C_{19}H_{31}IO_8$ (514.34): C, 44.37; H, 6.07. Found: C, 44.23; H, 5.95%.

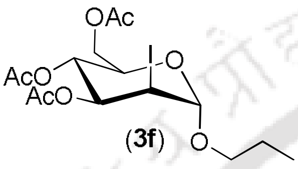
*Ethyl 3,4,6-tri-O-acetyl-2-deoxy-2-iodo-D-mannopyranoside (**3e**)*



(3e)

$[\alpha]_D^{25}$ +18° (*c* 0.07, CH_2Cl_2); **IR** (KBr) 2975, 2924, 1743, 1367, 1225, 1123, 1048 cm^{-1}; ^{1}**H NMR** (400 MHz, $CDCl_3$): δ 5.27 (t, *J* = 9.6 Hz, 1H), 5.09 (bs, 1H), 4.56 (dd, *J* = 9.2 Hz, *J* = 4.4 Hz, 1H), 4.43 (d, *J* = 4.4 Hz, 1H), 4.13 (dd, *J* = 12.0 Hz, *J* = 4.4 Hz, 1H), 4.04 (dd, *J* = 12.0 Hz, *J* = 2.4 Hz, 1H), 3.94 (ddd, *J* = 10.0 Hz, *J* = 4.8 Hz, *J* = 2.4 Hz, 1H), 3.66-3.62 (m, 1H), 3.48-3.43 (m, 1H), 2.02 (s, 3H), 1.99 (s, 3H), 1.96 (s, 3H), 1.15 (t, *J* = 6.8 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 170.7, 169.8, 169.5, 101.1, 69.1, 67.7, 64.1, 62.3, 29.8, 20.1, 20.8, 20.7, 15.0. **Anal. Calcd** for $C_{14}H_{21}IO_8$ (444.21): C, 37.85; H, 4.76. Found: C, 37.72; H, 4.64%.

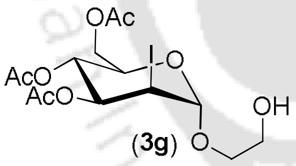
*Propyl 3,4,6-tri-O-acetyl-2-deoxy-2-iodo-D-mannopyranoside **(3f)***



(**3f**)

$[\alpha]_D^{25}$ +12° (*c* 0.062, CH_2Cl_2); **IR** (KBr) 2964, 2935, 1747, 1437, 1367, 1228, 1121, 1040, 949 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 5.36 (t, *J* = 10.0 Hz, 1H), 5.16 (bs, 1H), 4.64 (dd, *J* = 9.2 Hz, *J* = 4.0 Hz, 1H), 4.52 (d, *J* = 4.4 Hz, 1H), 4.22 (dd, *J* = 12.0 Hz, *J* = 4.8 Hz, 1H), 4.14 (dd, *J* = 12.4 Hz, *J* = 2.4 Hz, 1H), 4.01 (ddd, *J* = 10.0 Hz, *J* = 4.4 Hz, *J* = 2.0 Hz, 1H), 3.61 (dt, *J* = 9.6 Hz, *J* = 6.8 Hz, 1H), 3.42 (dt, *J* = 9.6 Hz, *J* = 6.4 Hz, 1H), 2.11 (s, 3H), 2.08 (s, 3H), 2.05 (s, 3H), 1.64-1.59 (m, 2H), 0.93 (t, *J* = 7.6 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 170.9, 170.0, 169.7, 101.5, 70.4, 69.3, 69.2, 67.8, 62.4, 29.9, 22.8, 21.1, 20.9, 20.8, 10.7. **Anal. Calcd** for $C_{15}H_{23}IO_8$ (458.24): C, 39.32; H, 5.06. Found: C, 39.20; H, 4.93%.

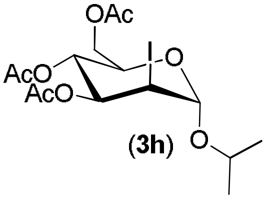
*2-Hydroxy ethyl 3,4,6-tri-O-acetyl-2-deoxy-2-iodo-D-mannopyranoside **(3g)***



(**3g**)

$[\alpha]_D^{25}$ +23° (*c* 0.022, CH_2Cl_2); **IR** (KBr) 3414, 2959, 2923, 2845, 1736, 1653, 1438, 1367, 1226, 1122, 1045 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 5.36 (t, *J* = 9.6 Hz, 1H), 5.19 (bs, 1H), 4.60 (dd, *J* = 9.2 Hz, *J* = 4.4 Hz, 1H), 4.52 (dd, *J* = 4.4 Hz, *J* = 1.2 Hz, 1H), 4.24 (dd, *J* = 12.4 Hz, *J* = 4.8 Hz, 1H), 4.12 (dd, *J* = 12.4 Hz, *J* = 2.0 Hz, 1H), 4.09-4.03 (m, 1H), 3.88-3.79 (m, 2H), 3.62-3.61 (m, 2H), 2.09 (s, 3H), 2.04 (s, 3H), 2.00 (s, 3H), 1.69 (bs, -OH, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 170.9, 169.8, 101.5, 69.5, 69.1, 67.6, 66.8, 62.3, 29.8, 21.1, 20.9. **Anal. Calcd** for $C_{14}H_{21}IO_9$ (460.21): C, 36.54; H, 4.60. Found: C, 36.42; H, 4.47%.

*Isopropyl 3,4,6-tri-O-acetyl-2-deoxy-2-iodo-D-mannopyranoside **(3h)***

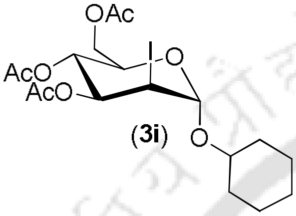


(**3h**)

$[\alpha]_D^{25}$ +17° (*c* 0.054, CH_2Cl_2); **IR** (KBr) 2973, 2928, 1746, 1437, 1368, 1226, 1117, 1036, 930, 838 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 5.29 (t, *J* = 9.6 Hz, 1H), 5.19 (bs, 1H), 4.59 (dd, *J* = 9.6 Hz, *J* = 4.0 Hz, 1H), 4.41 (d, *J* = 4.4 Hz, 1H), 4.15

(dd, *J* = 12.0 Hz, *J* = 4.4 Hz, 1H), 4.06 (dd, *J* = 12.4 Hz, *J* = 2.0 Hz, 1H), 4.02 (ddd, *J* = 10.0 Hz, *J* = 5.2 Hz, *J* = 2.4 Hz, 1H), 3.85-3.80 (m, 1H), 2.04 (s, 3H), 2.02 (s, 3H), 1.99 (s, 3H), 1.16 (d, *J* = 6.0 Hz, 3H), 1.10 (d, *J* = 6.4 Hz, 3H);**^{13}C NMR** (100 MHz, $CDCl_3$): δ 170.8, 170.0, 169.7, 99.7, 71.2, 69.3, 67.9, 62.5, 30.7, 23.2, 21.8, 21.1, 20.9, 20.8. **Anal. Calcd** for $C_{15}H_{23}IO_8$ (458.24): C, 39.32; H, 5.06. Found: C, 39.18; H, 4.95%.

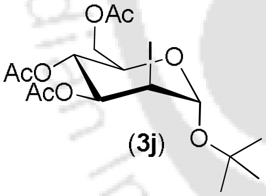
*Cyclohexyl 3,4,6-tri-O-acetyl-2-deoxy-2-iodo-D-mannopyranoside (**3i**)*



(3i)

$[\alpha]_D^{25}$ +27° (*c* 0.216, CH_2Cl_2); **IR** (KBr) 2933, 2855, 1748, 1449, 1367, 1228, 1116, 1039, 950, 601 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 5.34 (t, *J* = 9.6 Hz, 1H), 5.30 (bs, 1H), 4.66 (dd, *J* = 9.2 Hz, *J* = 4.0 Hz, 1H), 4.49 (dd, *J* = 4.4 Hz, *J* = 1.2 Hz, 1H), 4.22-4.16 (m, 2H), 4.11 (ddd, *J* = 10.0 Hz, *J* = 4.8 Hz, *J* = 2.4 Hz, 1H), 3.62-3.56 (m, 1H), 2.10 (s, 3H), 2.08 (s, 3H), 2.05 (s, 3H), 1.91-1.85 (m, 3H), 1.75-1.72 (m, 2H), 1.43-1.37 (m, 1H), 1.34-1.22 (m, 4H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 170.7, 169.9, 169.6, 99.6, 76.9, 69.2, 67.9, 62.4, 33.2, 31.6, 30.8, 25.5, 24.1, 23.9, 21.0, 20.7. **Anal. Calcd** for $C_{18}H_{27}IO_8$ (498.30): C, 43.39; H, 5.46. Found: C, 43.26; H, 5.34%.

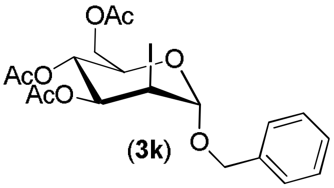
*t-Butyl 3,4,6-tri-O-acetyl-2-deoxy-2-iodo-D-mannopyranoside (**3j**)*



(3j)

$[\alpha]_D^{25}$ +10° (*c* 0.016, CH_2Cl_2); **IR** (KBr) 2970, 2922, 1743, 1639, 1368, 1226, 1111, 1043, 1017 cm^{-1}; **^{1}H NMR** (600 MHz, $CDCl_3$): δ 5.37 (bs, 1H), 5.32 (t, *J* = 9.0 Hz, 1H), 4.65 (dd, *J* = 9.0 Hz, *J* = 4.2 Hz, 1H), 4.37 (dd, *J* = 4.2 Hz, *J* = 1.2 Hz, 1H), 4.21-4.16 (m, 2H), 4.05 (dd, *J* = 11.4 Hz, *J* = 1.8 Hz, 1H), 2.06 (s, 3H), 2.05 (s, 3H), 2.02 (s, 3H), 1.23 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$): 170.9, 170.1, 169.7, 96.3, 77.0, 69.3, 68.9, 68.1, 62.6, 32.2, 28.5, 21.1, 20.9. **Anal. Calcd** for $C_{16}H_{25}IO_8$ (472.26): C, 40.69; H, 5.34. Found: C, 40.55; H, 5.23%.

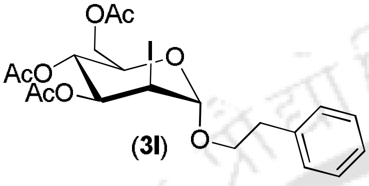
*Benzyl 3,4,6-tri-O-acetyl-2-deoxy-2-iodo-D-mannopyranoside (**3k**)*



(3k)

$[\alpha]_D^{25}$ +28° (*c* 0.18, CH_2Cl_2); **IR** (KBr) 2924, 2850, 1743, 1453, 1366, 1248, 1039, 749, 681 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.37-7.30 (m, 5H), 5.37 (t, *J* = 9.6 Hz, 1H), 5.23 (bs, 1H), 4.69 (d, *J* = 10 Hz, 1H), 4.65 (dd, *J* = 10.0 Hz, *J* = 4.4 Hz, 1H), 4.55 (dd, *J* = 4.0 Hz, *J* = 1 Hz, 1H), 4.53 (d, *J* = 10 Hz, 1H), 4.20 (dd, *J* = 12.0 Hz, *J* = 4.4 Hz, 1H), 4.06 (dd, *J* = 12.4 Hz, *J* = 2.3 Hz, 1H), 4.01 (ddd, *J* = 12.4 Hz, *J* = 4.4 Hz, *J* = 2.0 Hz, 1H), 2.11 (s, 3H), 2.06 (s, 3H), 2.03 (s, 3H); ^{13}**C NMR** (100 MHz, $CDCl_3$): δ 170.7, 169.9, 169.5, 136.4, 128.7, 128.3, 128.2, 100.5, 70.0, 69.3, 69.1, 67.5, 62.2, 29.6, 21.0, 20.8, 20.7. **Anal. Calcd** for $C_{19}H_{23}IO_8$ (506.28): C, 45.07; H, 4.58. Found: C, 44.92; H, 4.47%.

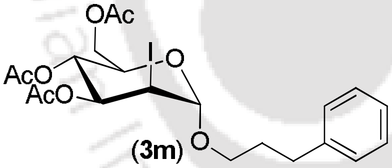
*2-Phenylethyl 3,4,6-tri-O-acetyl-2-deoxy-2-iodo-*D*-mannopyranoside* ***(3l)***



(3l)

$[\alpha]_D^{25}$ +21° (*c* 0.09, CH_2Cl_2); **IR** (KBr) 2920, 2845, 1744, 1367, 1224, 1120, 1046, 905, 701 cm^{-1}; ^{1}**H NMR** (400 MHz, $CDCl_3$): δ 7.31-7.19 (m, 5H), 5.28 (t, *J* = 9.6 Hz, 1H), 5.12 (bs, 1H), 4.56 (dd, *J* = 9.2 Hz, *J* = 4.0 Hz, 1H), 4.49 (dd, *J* = 4.4 Hz, *J* = 1.2 Hz, 1H), 4.04 (dd, *J* = 12.0 Hz, *J* = 4.4 Hz, 1H), 3.95 (dd, *J* = 12.0 Hz, *J* = 2.0 Hz, 1H), 3.82 (dt, *J* = 9.6 Hz, *J* = 6.8, Hz, 1H), 3.72 (dt, *J* = 9.2 Hz, *J* = 6.4 Hz, 1H), 3.46 (ddd, *J* = 10.0 Hz, *J* = 4.4 Hz, *J* = 2.4 Hz, 1H), 2.89 (t, *J* = 6.8 Hz, 2H), 2.07 (s, 6H), 2.02 (s, 3H); ^{13}**C NMR** (100 MHz, $CDCl_3$): δ 170.7, 169.9, 169.5, 138.6, 129.0, 128.6, 126.5, 100.9, 69.1, 69.06, 69.03, 67.4, 62.0, 36.1, 29.6, 21.0, 20.8, 20.7. **Anal. Calcd** for $C_{20}H_{25}IO_8$ (520.31): C, 46.17; H, 4.84. Found: C, 46.05; H, 4.75%.

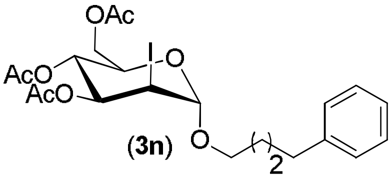
*3-Phenylpropyl 3,4,6-tri-O-acetyl-2-deoxy-2-iodo-*D*-mannopyranoside* ***(3m)***



(3m)

$[\alpha]_D^{25}$ +5° (*c* 0.25, CH_2Cl_2); **IR** (KBr) 3025, 2936, 2861, 1746, 1368, 1227, 1121, 1040, 910, cm^{-1}; ^{1}**H NMR** (400 MHz, $CDCl_3$): δ 7.26-7.22 (m, 5H), 5.35 (t, *J* = 9.6 Hz, 1H), 5.10 (bs, 1H), 4.64 (dd, *J* = 9.2 Hz, *J* = 4.4 Hz, 1H), 4.50 (dd, *J* = 4.4 Hz, *J* = 1.2 Hz, 1H), 4.17 (dd, *J* = 10.8 Hz, *J* = 4.8 Hz, 1H), 4.08 (dd, *J* = 12.0 Hz, *J* = 2.0 Hz, 1H), 3.94 (ddd, *J* = 10.0 Hz, *J* = 4.8 Hz, *J* = 2.4 Hz, 1H), 3.59 (t, *J* = 6.4 Hz, 2H), 2.65 (t, *J* = 7.6 Hz, 2H), 2.05 (s, 3H), 2.03 (s, 3H), 2.02 (s, 3H), 1.93-1.83 (m, 2H); ^{13}**C NMR** (100 MHz, $CDCl_3$): δ 171.1, 170.2, 169.9, 141.4, 128.7, 128.6, 126.2, 101.5, 69.4, 69.3, 68.0, 67.8, 62.5, 32.4, 30.9, 29.9, 21.1, 21.0, 20.9. **Anal. Calcd** for $C_{21}H_{27}IO_8$ (534.33): C, 47.20; H, 5.09. Found: C, 47.06; H, 4.96%.

*4-Phenylbutyl 3,4,6-tri-O-acetyl-2-deoxy-2-iodo-*D*-mannopyranoside* ***(3n)***

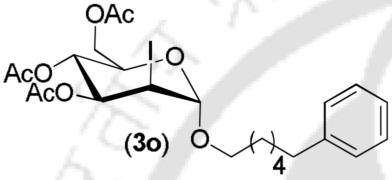


(3n)

$[\alpha]_D^{25}$ +10° (*c* 0.19, CH_2Cl_2); **IR** (KBr) 3025, 2936, 2858, 1748, 1653, 1495, 1453, 1367, 1227, 1120, 1043, 748 cm^{-1}; ^{1}**H NMR** (600 MHz, $CDCl_3$): δ 7.29-

7.26 (m, 2H), 7.20-7.17 (m, 3H), 5.35 (t, J = 9.6 Hz, 1H), 5.14 (bs, 1H), 4.63 (dd, J = 9.6 Hz, J = 4.8 Hz, 1H), 4.51 (dd, J = 4.8 Hz, J = 1.2 Hz, 1H), 4.20 (dd, J = 12.0 Hz, J = 4.8 Hz, 1H), 4.12 (dd, J = 12.6 Hz, J = 2.4 Hz, 1H), 3.99 (m, 1H), 3.68-3.65 (m, 1H), 3.46-3.45 (m, 1H), 2.64 (t, J = 7.8 Hz, 2H), 2.09 (s, 3H), 2.07 (s, 3H), 2.04 (s, 3H), 1.71-1.62 (m, 4H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 170.8, 170.0, 169.6, 142.1, 128.6, 128.5, 126.0, 101.4, 69.3, 69.2, 68.6, 67.7, 62.4, 35.7, 29.8, 29.0, 28.0, 21.1, 20.9, 20.8. **Anal. Calcd** for $C_{22}H_{29}IO_8$ (548.36): C, 48.19; H, 5.33. Found: C, 48.04; H, 5.25%.

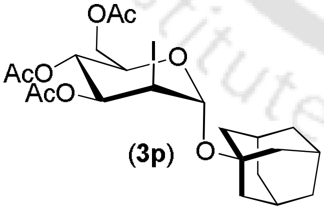
6-Phenylhexyl 3,4,6-tri-O-acetyl-2-deoxy-2-iodo-ᴅ-mannopyranoside ***(3o)***



(3o)

[α]$_D^{25}$ +13° (c 0.09, CH_2Cl_2); **IR** (KBr) 2927, 2848, 1751, 1654, 1366, 1226, 1121, 1044, 744 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.23-7.15 (m, 5H), 5.29 (t, J = 9.6 Hz, 1H), 5.07 (bs, 1H), 4.56 (dd, J = 9.2 Hz, J = 4.4 Hz, 1H), 4.44 (d, J = 4.4 Hz, 1H), 4.14 (dd, J = 12.0 Hz, J = 4.0 Hz, 1H), 4.05 (dd, J = 12.4 Hz, J = 2.0 Hz, 1H), 3.92 (ddd, J = 10.0 Hz, J = 4.8 Hz, J = 2.4 Hz, 1H), 3.59-3.51 (m, 1H), 3.38-3.34 (m, 1H), 2.55-2.50 (m, 2H), 2.02 (s, 3H), 2.00 (s, 3H), 1.97 (s, 3H), 1.56-1.46 (m, 4H), 1.29-1.28 (m, 4H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 170.9, 170.1, 169.7, 142.9, 128.6, 128.4, 125.8, 101.5, 69.3, 68.8, 67.8, 63.1, 62.5, 36.0, 31.5, 29.9, 29.5, 29.2, 25.8, 21.1, 20.9, 20.8. **Anal. Calcd** for $C_{24}H_{33}IO_8$ (576.41): C, 50.01; H, 5.77. Found: C, 49.87; H, 5.62%.

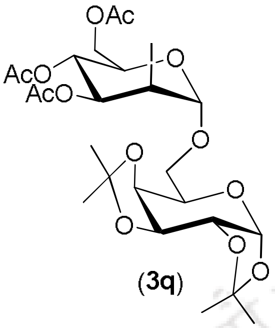
Adamantyl 3,4,6-tri-O-acetyl-2-deoxy-2-iodo-ᴅ-mannopyranoside ***(3p)***



(3p)

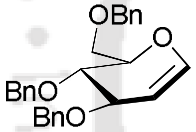
[α]$_D^{25}$ +13° (c 0.124, CH_2Cl_2); **IR** (KBr) 2909, 2851, 1748, 1451, 1367, 1228, 1034, 963 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 5.45 (bs, 1H), 5.27 (t, J = 9.6 Hz, 1H), 4.63 (dd, J = 9.6 Hz, J = 4.4 Hz, 1H), 4.33 (dd, J = 4.0 Hz, J = 1.2 Hz, 1H), 4.17-4.12 (m, 2H), 4.03 (dd, J = 11.6 Hz, J = 2.0 Hz, 1H), 2.08-2.06 (m, 4H), 2.02 (s, 3H), 2.00 (s, 3H), 1.98 (s, 3H), 1.73 (bs, 3H), 1.65-1.64 (m, 4H), 1.55-1.53 (m, 4H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 170.7, 169.9, 169.5, 94.7, 76.2, 69.2, 68.7, 68.0, 62.4, 42.3, 32.2, 30.6, 21.0, 20.7, 20.6. **Anal. Calcd** for $C_{22}H_{31}IO_8$ (550.38): C, 48.01; H, 5.68. Found: C, 47.92; H, 5.56%.

*6-O-(3,4,6-tri-O-acetyl-2-deoxy-2-iodo-α-D-mannopyranosyl)-1,2,3,4-di-O-isopropylidene-α-D-galactopyranoside **(3q)***


(**3q**)

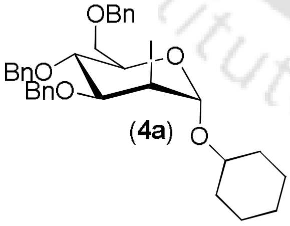
$[\alpha]_D^{25}$ -37° (*c* 0.042, CH_2Cl_2); **IR** (KBr) 2984, 2926, 2845, 1751, 1377, 1369, 1227, 1122, 1067, 1004, 891 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 5.50 (d, *J* = 5.2 Hz, 1H), 5.37 (t, *J* = 9.6 Hz, 1H), 5.24 (bs, 1H), 4.63-4.60 (m, 2H), 4.57 (dd, *J* = 4.8 Hz, *J* = 1.2 Hz, 1H), 4.32 (dd, *J* = 4.8 Hz, *J* = 2.4 Hz, 1H), 4.26-4.22 (m, 2H), 4.15-4.11 (m, 2H), 3.96 (ddd, *J* = 13.2 Hz, *J* = 6.4 Hz, *J* = 2.0 Hz, 1H), 3.79 (dd, *J* = 10.4 Hz, *J* = 6.4 Hz, 1H), 3.71 (dd, *J* = 10.0 Hz, *J* = 6.0 Hz, 1H), 2.12 (s, 3H), 2.08 (s, 3H), 2.05 (s, 3H), 1.55 (s, 3H), 1.43 (s, 3H), 1.34 (s, 6H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 171.0, 170.0, 169.7, 109.6, 108.9, 101.5, 96.4, 71.0, 70.8, 70.7, 69.4, 69.3, 67.6, 67.1, 66.3, 62.3, 29.7, 26.3, 26.1, 25.1, 24.7, 21.1, 20.9, 20.8.

*3,4,6-Tri-O-benzyl-D-glucal **(4)***


(**4**)

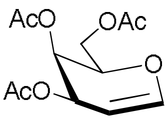
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.39-7.26 (m, 15H), 6.49 (d, *J* = 6.0 Hz, 1H), 4.93 (dd, *J* = 6.0 Hz, *J* = 2.4 Hz, 1H), 4.90 (d, *J* = 11.4 Hz, 1H), 4.72-4.68 (m, 2H), 4.66-4.60 (m, 3H), 4.28-4.27 (m, 1H), 4.14-4.11 (m, 1H), 3.93 (dd, *J* = 8.4 Hz, *J* = 6.0 Hz, 1H), 3.87 (dd, *J* = 10.2 Hz, *J* = 4.8 Hz, 1H), 3.82 (dd, *J* = 10.8 Hz, *J* = 2.4 Hz, 1H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 144.8, 138.5, 138.3, 138.1, 128.5, 128.0, 127.9, 127.8, 127.7, 100.1, 76.9, 75.8, 74.5, 73.8, 73.6, 70.5, 68.6.

*Cyclohexyl 3,4,6-tri-O-benzyl-2-deoxy-2-iodo-D-mannopyranoside **(4a)***


(**4a**)

$[\alpha]_D^{25}$ +8° (*c* 0.050, CH_2Cl_2); **IR** (KBr) 3062, 3029, 2929, 2854, 1496, 1452, 1362, 1290, 1258, 1207, 1116, 1045, 1027, 999, 733, 696 cm^{-1}; **^{1}H NMR** (600 MHz, $CDCl_3$): δ 7.34 (d, *J* = 7.2 Hz, 2H), 7.30-7.17 (m, 11H), 7.09 (dd, *J* = 7.8 Hz, *J* = 1.8 Hz, 2H), 5.27 (bs, 1H), 4.77 (d, *J* = 10.8 Hz, 1H), 4.63 (t, *J* = 12.0 Hz, 2H), 4.46-4.39 (m, 4H), 3.88-3.81 (m, 2H), 3.72 (dd, *J* = 10.8 Hz, *J* = 4.8 Hz, 1H), 3.62 (dd, *J* = 10.8 Hz, *J* = 1.2 Hz, 1H), 3.53-3.49 (m, 1H), 3.27 (dd, *J* = 8.4 Hz, *J* = 3.6 Hz, 1H), 1.75-1.74 (m, 2H), 1.61-1.59 (m, 2H), 1.43-1.41 (m, 1H), 1.18-1.14 (m, 5H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 138.6, 138.4, 138.0, 128.6, 128.5, 128.4, 128.3, 128.2, 128.0, 127.9, 127.8, 127.6, 99.6, 77.0, 76.3, 75.9, 75.5, 73.5, 72.3, 71.1, 69.2, 34.9, 33.4, 31.7, 25.7, 24.2, 24.0. **Anal. Calcd** for $C_{33}H_{39}IO_5$ (642.56): C, 61.68; H, 6.12. Found: C, 61.55; H, 6.02%.

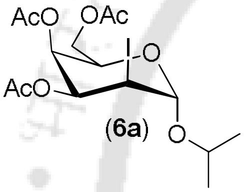
*3,4,6-Tri-O-acetyl-D-galactal (**5**)*



(**5**)

$[\alpha]_D^{25}$ -14° (*c* 0.136, CH_2Cl_2); **IR** (KBr) 1747, 1652, 1437, 1372, 1225, 1148, 1080, 1064, 1035 cm^{-1}; **^{1}H NMR** (600 MHz, $CDCl_3$): δ 6.44 (dd, *J* = 6.6 Hz, *J* = 1.8 Hz, 1H), 5.53 (dd, *J* = 3.0 Hz, *J* = 1.2 Hz, 1H), 5.40 (dd, *J* = 4.8 Hz, *J* = 2.4 Hz, 1H), 4.71 (dd, *J* = 7.2 Hz, *J* = 1.2 Hz, 1H), 4.31-4.20 (m, 3H), 2.10 (s, 3H), 2.06 (s, 3H), 2.00 (s, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 170.7, 170.5, 170.3, 145.6, 99.0, 72.9, 64.0, 63.9, 62.1, 21.0, 20.9, 20.8.

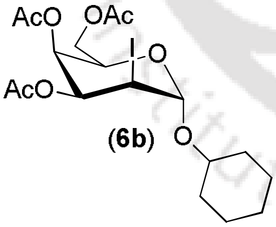
*Isopropyl 3,4,6-tri-O-acetyl-2-deoxy-2-iodo-D-talopyranoside (**6a**)*



(**6a**)

^{1}H NMR (600 MHz, $CDCl_3$): δ 5.38 (bs, 1H), 5.36 (t, *J* = 2.4 Hz, 1H), 4.92 (t, *J* = 4.2 Hz, 1H), 4.36-4.33 (m, 1H), 4.21 (d, *J* = 4.2 Hz, 1H), 4.19-4.13 (m, 2H), 3.92-3.88 (m, 1H), 2.16 (s, 3H), 2.05 (s, 3H), 2.03 (s, 3H), 1.21 (d, *J* = 6.6 Hz, 3H), 1.16 (d, *J* = 6.0 Hz, 3H);**^{13}C NMR** (150 MHz, $CDCl_3$): δ 170.6, 170.3, 169.7, 101.2, 71.2, 66.9, 65.7, 65.5, 62.3, 23.2, 22.6, 21.9, 21.2, 21.0, 20.8. **Anal. Calcd** for $C_{15}H_{23}IO_8$ (458.24): C, 39.32; H, 5.06. Found: C, 39.20; H, 4.93%.

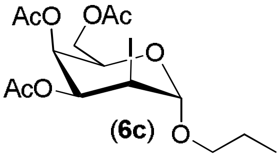
*Cyclohexyl 3,4,6-tri-O-acetyl-2-deoxy-2-iodo-D-talopyranoside (**6b**)*



(**6b**)

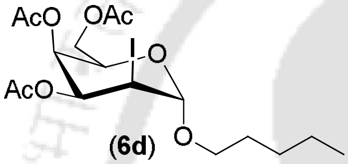
$[\alpha]_D^{25}$ +46° (*c* 0.062, CH_2Cl_2); **IR** (KBr) 2933, 2856, 1750, 1371, 1227, 1110, 1047, 987 cm^{-1}; **^{1}H NMR** (600 MHz, $CDCl_3$): δ 5.41 (bs, 1H), 5.35 (bs, 1H), 4.92 (t, *J* = 4.8 Hz, 1H), 4.35 (t, *J* = 6.6 Hz, 1H), 4.21 (d, *J* = 4.8 Hz, 1H), 4.14 (dd, *J* = 8.4 Hz, *J* = 1.8 Hz, 2H), 3.58-3.55 (m, 1H), 2.15 (s, 3H), 2.04 (s, 3H), 2.01 (s, 3H), 1.84 (bs, 2H), 1.71 (bs, 2H), 1.52-1.51 (m, 1H), 1.39-1.31 (m, 1H), 1.28-1.17 (m, 4H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 170.3, 170.0, 169.4, 100.8, 76.7, 66.6, 65.5, 65.3, 62.0, 33.1, 31.5, 25.4, 24.1, 23.8, 22.5, 20.9, 20.8, 20.6. **Anal. Calcd** for $C_{18}H_{27}IO_8$ (498.30): C, 43.39; H, 5.46. Found: C, 43.28; H, 5.32%.

*Propyl 3,4,6-tri-O-acetyl-2-deoxy-2-iodo-D-talopyranoside **(6c)***


(6c)

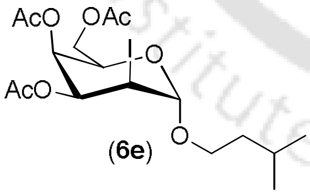
$[\alpha]_D^{25}$ +38° (*c* 0.110, CH_2Cl_2); **IR** (KBr) 2964, 2926, 1750, 1372, 1228, 1170, 1116, 1049, 989, 727 cm^{-1}; **^{1}H NMR** (600 MHz, $CDCl_3$): δ 5.35 (bs, 1H), 5.29 (bs, 1H), 4.90 (t, *J* = 4.8 Hz, 1H), 4.27-4.24 (m, 2H), 4.18-4.13 (m, 2H), 3.60 (dt, *J* = 9.6 Hz, *J* = 6.6 Hz, 1H), 3.40 (dt, *J* = 9.6 Hz, *J* = 6.6 Hz, 1H), 2.15 (s, 3H), 2.04 (s, 3H), 2.02 (s, 3H), 1.60-1.57 (m, 2H), 0.91 (t, *J* = 7.8 Hz, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 170.6, 170.2, 169.7, 102.7, 70.3, 66.7, 65.6, 65.4, 62.2, 22.8, 21.7, 21.1, 21.0, 20.8, 10.7. **Anal. Calcd** for $C_{15}H_{23}IO_8$ (458.24): C, 39.32; H, 5.06. Found: C, 39.22; H, 4.94%.

*Pentyl 3,4,6-tri-O-acetyl-2-deoxy-2-iodo-D-talopyranoside **(6d)***


(6d)

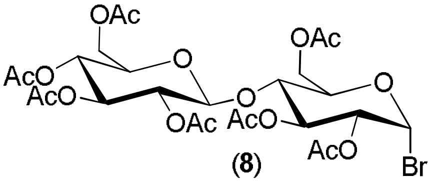
$[\alpha]_D^{25}$ +30° (*c* 0.214, CH_2Cl_2); **IR** (KBr) 2957, 2927, 1750, 1370, 1225, 1111, 1051, 971 cm^{-1}; **^{1}H NMR** (600 MHz, $CDCl_3$): δ 5.37 (bs, 1H), 5.29 (bs, 1H), 4.91 (t, *J* = 4.2 Hz, 1H), 4.28-4.25 (m, 2H), 4.19-4.13 (m, 2H), 3.65 (dt, *J* = 9.6 Hz, *J* = 6.6 Hz, 1H), 3.44 (dt, *J* = 9.6 Hz, *J* = 6.6 Hz, 1H), 2.17 (s, 3H), 2.06 (s, 3H), 2.05 (s, 3H), 1.60-01.55 (m, 2H), 1.31-1.30 (m, 4H), 0.89 (t, *J* = 7.2 Hz, 3H);**^{13}C NMR** (100 MHz, $CDCl_3$): δ 170.6, 170.3, 169.7, 102.7, 68.7, 66.7, 65.6, 65.4, 62.3, 29.2, 28.4, 22.5, 21.7, 21.1, 21.0, 20.8, 14.1. **Anal. Calcd** for $C_{17}H_{27}IO_8$ (486.29): C, 41.99; H, 5.60. Found: C, 41.89; H, 5.48%.

*Isopentyl 3,4,6-tri-O-acetyl-2-deoxy-2-iodo-D-talopyranoside **(6e)***


(6e)

$[\alpha]_D^{25}$ +35° (*c* 0.098, CH_2Cl_2); **IR** (KBr) 2957, 2928, 2872, 1750, 1467, 1371, 1229, 1113, 1054, 965, 728, 602 cm^{-1}; **^{1}H NMR** (600 MHz, $CDCl_3$): δ 5.36 (bs, 1H), 5.28 (bs, 1H), 4.89 (t, *J* = 4.2 Hz, 1H), 4.27-4.23 (m, 2H), 4.19-4.12 (m, 2H), 3.69 (dt, *J* = 9.6 Hz, *J* = 6.6 Hz, 1H), 3.46 (dt, *J* = 9.6 Hz, *J* = 6.6 Hz, 1H), 2.16 (s, 3H), 2.04 (s, 3H), 2.02 (s, 3H), 1.69-1.65 (m, 1H), 1.48-1.44 (m, 2H), 0.89 (d, *J* = 6.6 Hz, 6H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 170.6, 170.3, 169.7, 102.8, 67.1, 66.9, 65.6, 65.5, 62.4, 38.3, 25.1, 22.8, 22.5, 21.8, 21.1, 21.0, 20.8. **Anal. Calcd** for $C_{17}H_{27}IO_8$ (486.29): C, 41.99; H, 5.60. Found: C, 41.87; H, 5.46%.

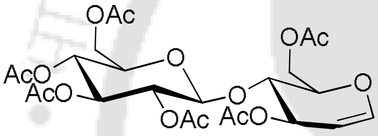
2,2',3,3',4',6,6'-Hepta-O-acetyl-α-bromo-ᴅ-cellobiose ***(8)***



(8)

$[\alpha]_D^{25}$ +95° (*c* 0.200, CH_2Cl_2); **IR** (KBr) 2956, 2923, 2852, 1752, 1736, 1366, 1214, 1033, 902, 597 cm^{-1}; ^{1}**H NMR** (600 MHz, $CDCl_3$): δ 6.51 (d, *J* = 3.6 Hz, 1H), 5.52 (t, *J* = 9.6 Hz, 1H), 5.14 (t, *J* = 9.0 Hz, 1H), 5.06 (t, *J* = 10.2 Hz, 1H), 4.92 (t, *J* = 9.0 Hz, 1H), 4.75 (dd, *J* = 10.2 Hz, *J* = 4.2 Hz, 1H), 4.52 (dd, *J* = 10.8 Hz, *J* = 7.8 Hz, 2H), 4.35 (dd, *J* = 12.6 Hz, *J* = 4.8 Hz, 1H), 4.20-4.15 (m, 2H), 4.04 (dd, *J* = 12.6 Hz, *J* = 1.8 Hz, 1H), 3.83 (t, *J* = 9.6 Hz, 1H), 3.68-3.67 (m, 1H), 2.12 (s, 3H), 2.08 (s, 6H), 2.03 (s, 6H), 2.00 (s, 3H), 1.97 (s, 3H). ^{13}**C NMR** (150 MHz, $CDCl_3$): δ 170.6, 170.4, 170.3, 170.2, 169.5, 169.1, 100.7, 86.6, 75.4, 73.2, 73.1, 72.2, 71.8, 70.9, 69.6, 68.0, 61.8, 61.1, 21.0, 20.9, 20.8, 20.7.

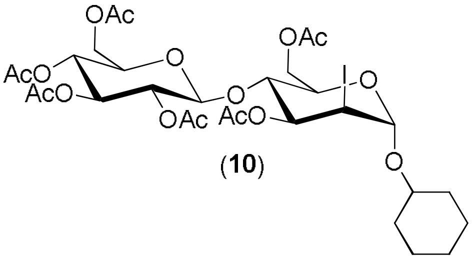
3,6,2',3',4',6'-Hexa-O-acetyl-ᴅ-cellobial ***(9)***



(**9**)

IR (KBr) 2959, 1743, 1651, 1436, 1369, 1226, 1166, 1062, 1037, 907 cm^{-1}; ^{1}**H NMR** (400 MHz, $CDCl_3$): δ 6.36 (dd, *J* = 6.0 Hz, *J* = 1.2 Hz, 1H), 5.38-5.36 (m, 1H), 5.14 (t, *J* = 9.2 Hz, 1H), 5.03 (t, *J* = 9.6 Hz, 1H), 4.95-4.90 (m, 1H), 4.77 (dd, *J* = 6.0 Hz, *J* = 3.2 Hz, 1H), 4.65 (d, *J* = 8.0 Hz, 1H), 4.40 (dd, *J* = 11.2 Hz, *J* = 2.0 Hz, 1H), 4.26 (dd, *J* = 12.4 Hz, *J* = 4.4 Hz, 1H), 4.16-4.12 (m, 1H), 4.10-4.08 (m, 1H), 4.02 (dd, *J* = 12.4 Hz, *J* = 2.4 Hz, 1H), 3.94 (dd, *J* = 7.2 Hz, *J* = 5.2 Hz, 1H), 3.67-3.63 (m, 1H), 2.07 (s, 3H), 2.04 (s, 3H), 2.01 (s, 3H), 2.00 (s, 3H), 1.97 (s, 3H), 1.95 (s, 3H). ^{13}**C NMR** (100 MHz, $CDCl_3$): δ 170.3, 170.1, 169.9, 169.7, 169.1, 168.9, 145.2, 100.3, 98.9, 74.4, 74.2, 72.5, 71.7, 71.2, 68.5, 67.9, 61.6, 20.7, 20.5, 20.4, 20.3. **Anal. Calcd** for $C_{24}H_{32}O_{15}$ (560.50): C, 51.43; H, 5.75. Found: C, 51.31; H, 5.61%.

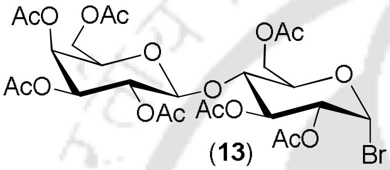
Cyclohexyl 3,6-Di-O-acetyl-4-O-(2,3,4,6,-tetra-O-acetyl-β-ᴅ-glucopyranosyl)-2-deoxy-2-iodo-ᴅ-mannopyranoside ***(10)***



(**10**)

$[\alpha]_D^{25}$ +22.3° (*c* 0.596, CH_2Cl_2); **IR** (KBr) 2934, 2857, 1750, 1450, 1368, 1230, 1167, 1117, 1039, 906 cm^{-1}; ^{1}**H NMR** (600 MHz, $CDCl_3$): δ 5.22 (d, *J* = 1.2 Hz, 1H), 5.15 (t, *J* = 9.6 Hz, 1H), 5.04 (t, *J* = 9.6 Hz, 1H), 4.92 (dd, *J* = 9.0 Hz, *J* = 7.8 Hz, 1H), 4.69 (dd, *J* = 7.8 Hz, *J* = 3.6 Hz, 1H), 4.59 (d, *J* = 7.8 Hz, 1H), 4.44-4.41 (m, 2H), 4.29 (dd, *J* = 12.6 Hz, *J* = 5.4 Hz, 1H), 4.09 (dd, *J* = 11.4 Hz, *J* = 4.8 Hz, 1H), 4.05 (dd, *J* = 12.6 Hz, *J* = 2.4 Hz, 1H), 4.00-3.98 (m, 1H), 3.92 (t, *J* = 8.4 Hz, 1H), 3.70 (ddd, *J* = 10.2 Hz, *J* = 5.4 Hz, *J* = 2.4 Hz, 1H), 3.53-3.52 (m, 1H), 2.10 (s, 3H), 2.09 (s, 3H), 2.08 (s, 3H), 2.03 (s, 3H), 2.00 (s, 3H), 1.97 (s, 3H), 1.84-1.79 (m, 3H), 1.71-1.70 (m, 2H), 1.38-1.36 (m, 1H), 1.27-1.18 (m, 4H). **^{13}C NMR** (100 MHz, CDCl$_3$): δ 170.3, 170.2, 169.9, 169.2, 169.1, 169.0, 100.8, 99.3, 76.7, 76.2, 72.8, 71.6, 71.5, 69.4, 69.2, 67.9, 62.1, 61.8, 33.0, 31.4, 29.4, 25.3, 23.9, 23.7, 20.8, 20.7, 20.6, 20.4. **Anal. Calcd** for $C_{30}H_{43}IO_{16}$ (786.55): C, 45.81; H, 5.51. Found: C, 45.67; H, 5.40%.

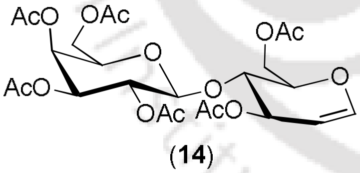
2,2',3,3',4',6,6'-Hepta-O-acetyl-α-bromo-D-lactose ***(13)***



(**13**)

^{1}H NMR (400 MHz, CDCl$_3$): δ 6.49 (d, *J* = 4.0 Hz, 1H), 5.52 (t, *J* = 9.6 Hz, 1H), 5.32 (d, *J* = 2.8 Hz, 1H), 5.09 (dd, *J* = 10.8 Hz, *J* = 8.0 Hz, 1H), 4.92 (dd, *J* = 10.0 Hz, *J* = 3.2 Hz, 1H), 4.72 (dd, *J* = 10.4 Hz, *J* = 4.0 Hz, 1H), 4.48-4.45 (m, 2H), 4.17-4.09 (m, 3H), 4.04 (dd, *J* = 11.2 Hz, *J* = 7.6 Hz, 1H), 3.87-3.80 (m, 2H), 2.13 (s, 3H), 2.10 (s, 3H), 2.06 (s, 3H), 2.04 (s, 3H), 2.03 (s, 3H), 2.02 (s, 3H), 1.93 (s, 3H). **^{13}C NMR** (150 MHz, CDCl$_3$): δ 170.6, 170.4, 170.3 (2C), 170.2, 169.5, 169.2, 100.9, 86.6, 75.1, 73.2, 71.2, 71.0 (2C), 69.8, 69.2, 66.8, 61.2, 61.1, 21.0, 20.8, 20.7.

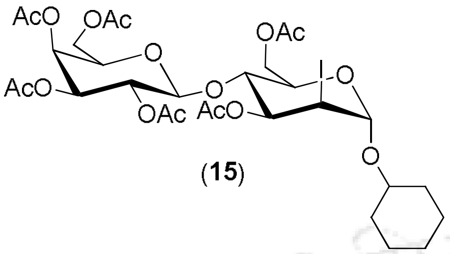
3,6,2',3',4',6'-Hexa-O-acetyl-D-lactal ***(14)***



(**14**)

$[\alpha]_D^{25}$ +33° (*c* 0.138, CH$_2$Cl$_2$); **IR** (KBr) 2926, 1746, 1432, 1370, 1234, 1133, 1051, 906 cm^{-1}; **^{1}H NMR** (600 MHz, CDCl$_3$): δ 6.37 (d, *J* = 6.6 Hz, 1H), 5.37 (t, *J* = 3.6 Hz, 1H), 5.32 (d, *J* = 3.0 Hz, 1H), 5.15 (dd, *J* = 10.8 Hz, *J* = 7.8 Hz, 1H), 4.97 (dd, *J* = 10.2 Hz, *J* = 3.0 Hz, 1H), 4.80 (dd, *J* = 6.6 Hz, *J* = 3.6 Hz, 1H), 4.63 (d, *J* = 7.8 Hz, 1H), 4.40 (dd, *J* = 12.0 Hz, *J* = 2.4 Hz, 1H), 4.16 (dd, *J* = 11.4 Hz, *J* = 6.0 Hz, 1H), 4.13-4.10 (m, 2H), 4.04 (dd, *J* = 11.4 Hz, *J* = 7.2 Hz, 1H), 3.96 (dd, *J* = 7.2 Hz, *J* = 5.4 Hz, 1H), 3.88 (t, *J* = 6.6 Hz, 1H) 2.12 (s, 3H), 2.08 (s, 3H), 2.05 (s, 3H), 2.03 (s, 3H), 2.01 (s, 3H), 1.94 (s, 3H). **^{13}C NMR** (150 MHz, CDCl$_3$): δ 170.5, 170.3, 170.2, 170.0, 169.4, 145.6, 101.1, 99.1, 74.8, 74.3, 71.0, 70.8, 69.0, 68.9, 66.8, 61.9, 61.1, 21.2, 20.9, 20.8, 20.7, 20.6. **Anal. Calcd** for $C_{24}H_{32}O_{15}$ (560.50): C, 51.43; H, 5.75. Found: C, 51.33; H, 5.64%.

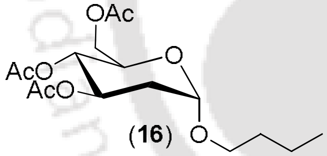
*Cyclohexyl 3,6-Di-O-acetyl-4-O-(2,3,4,6,-tetra-O-acetyl-β-D-galactopyranosyl)-2-deoxy-2-iodo-D-mannopyranoside (**15**)*



(**15**)

$[\alpha]_D^{25}$ +26° (c 0.052, CH_2Cl_2); **IR** (KBr) 2928, 2854, 1750, 1369, 1222, 1118, 1080, 1046, 954, 602 cm^{-1}; **^{1}H NMR** (600 MHz, $CDCl_3$): δ 5.34 (d, J = 3.0 Hz, 1H), 5.22 (d, J = 1.8 Hz, 1H), 5.13 (dd, J = 10.2 Hz, J = 7.8 Hz, 1H), 4.97 (dd, J = 10.8 Hz, J = 3.6 Hz, 1H), 4.72 (dd, J = 7.8 Hz, J = 4.2 Hz, 1H), 4.59 (d, J = 8.4 Hz, 1H), 4.46-4.45 (m, 1H), 4.39 (dd, J = 12.0 Hz, J = 1.8 Hz, 1H), 4.14 (dd, J = 11.4 Hz, J = 6.6 Hz, 1H), 4.10-4.05 (m, 2H), 4.01-3.99 (m, 1H), 3.95-3.89 (m, 2H), 3.55-3.51 (m, 1H), 2.13 (s, 3H), 2.11 (s, 3H), 2.09 (s, 3H), 2.05 (s, 6H), 1.95 (s, 3H), 1.84-1.79 (m, 2H), 1.71-1.69 (m, 2H), 1.50-1.49 (m, 1H), 1.37-1.34 (m, 1H), 1.26-1.20 (m, 4H). **^{13}C NMR** (150 MHz, $CDCl_3$): δ 170.7, 170.6, 170.3, 170.2, 169.6, 169.5, 101.6, 99.7, 77.0, 76.4, 71.2, 70.8, 70.2, 69.5, 69.4, 67.0, 62.5, 61.4, 33.3, 31.7, 29.8, 25.6, 24.2, 24.0, 21.3, 21.0, 20.9, 20.8, 20.7. **Anal. Calcd** for $C_{30}H_{43}IO_{16}$ (786.55): C, 45.81; H, 5.51. Found: C, 45.69; H, 5.38%.

*Butyl 3,4,6-tri-O-acetyl-2-deoxy-D-glucopyranoside (**16**)*



(**16**)

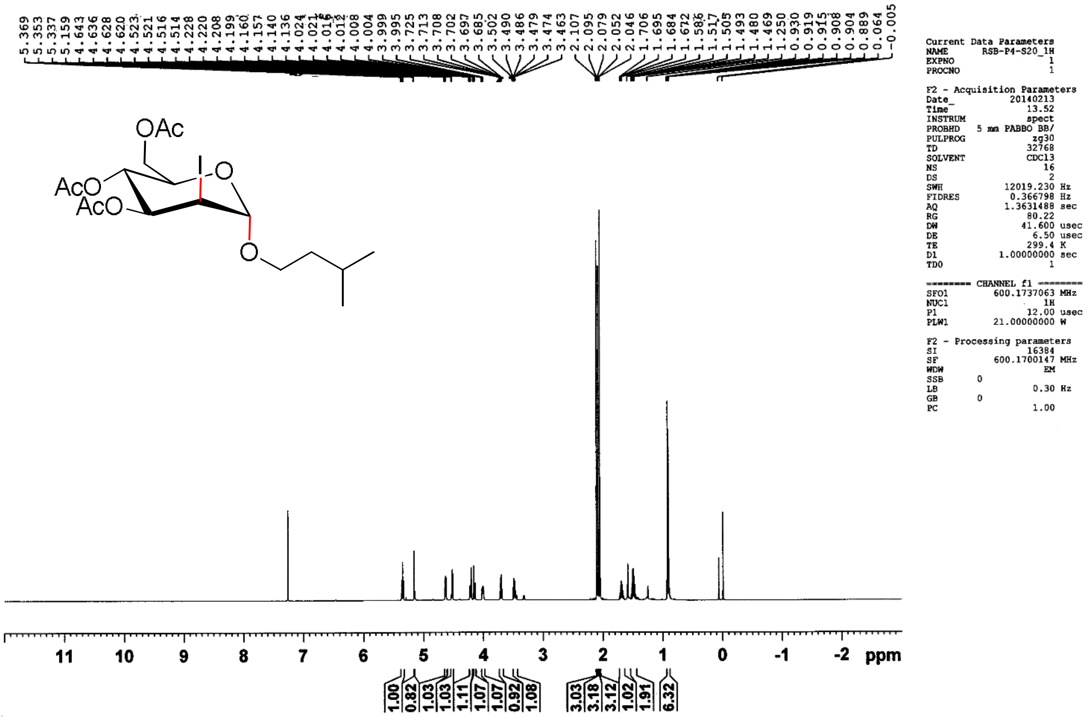
$[\alpha]_D^{25}$ +104° (c 0.047, CH_2Cl_2); **IR** (KBr) 2959, 2925, 2867, 1745, 1438, 1367, 1229, 1129, 1047 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 5.24 (ddd, J = 14.8 Hz, J = 9.6 Hz, J = 5.6 Hz, 1H), 4.91 (t, J = 9.6 Hz, 1H), 4.86 (d, J = 3.2 Hz, 1H), 4.22 (dd, J = 12.0 Hz, J = 4.0 Hz, 1H), 3.98 (dd, J = 12.0 Hz, J = 2.0 Hz, 1H), 3.89 (ddd, J = 10.4 Hz, J = 4.8 Hz, J = 2.4 Hz, 1H), 3.56 (dt, J = 9.6 Hz, J = 6.8 Hz, 1H), 3.32 (dt, J = 9.6 Hz, J = 6.4 Hz, 1H), 2.15 (ddd, J = 12.0 Hz, J = 5.6 Hz, J = 1.2 Hz, 1H), 2.01 (s, 3H), 1.97 (s, 3H), 1.94 (s, 3H), 1.74 (ddd, J = 15.2 Hz, J = 11.6 Hz, J = 3.6 Hz, 1H), 1.52-1.46 (m, 2H), 1.34-1.28 (m, 2H), 0.86 (t, J = 7.2 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 170.8, 170.3, 170.0, 97.0, 69.6, 69.3, 67.8, 67.6, 62.6, 35.2, 31.5, 21.0, 20.8, 19.4, 13.9. **Anal. Calcd** for $C_{16}H_{26}O_8$ (346.37): C, 55.48; H, 7.57. Found: C, 55.34; H, 7.45%.

Complete crystallographic data of **6a** & **10** for the structural analyses have been deposited with the Cambridge Crystallographic Data Centre, CCDC No. 1006142 and 1006157. Copies of this information may be obtained free of charge from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK, (fax: +44-1223-336033, e-mail: deposit@ccdc.cam.ac.uk or via: www.ccdc.cam.ac.uk).

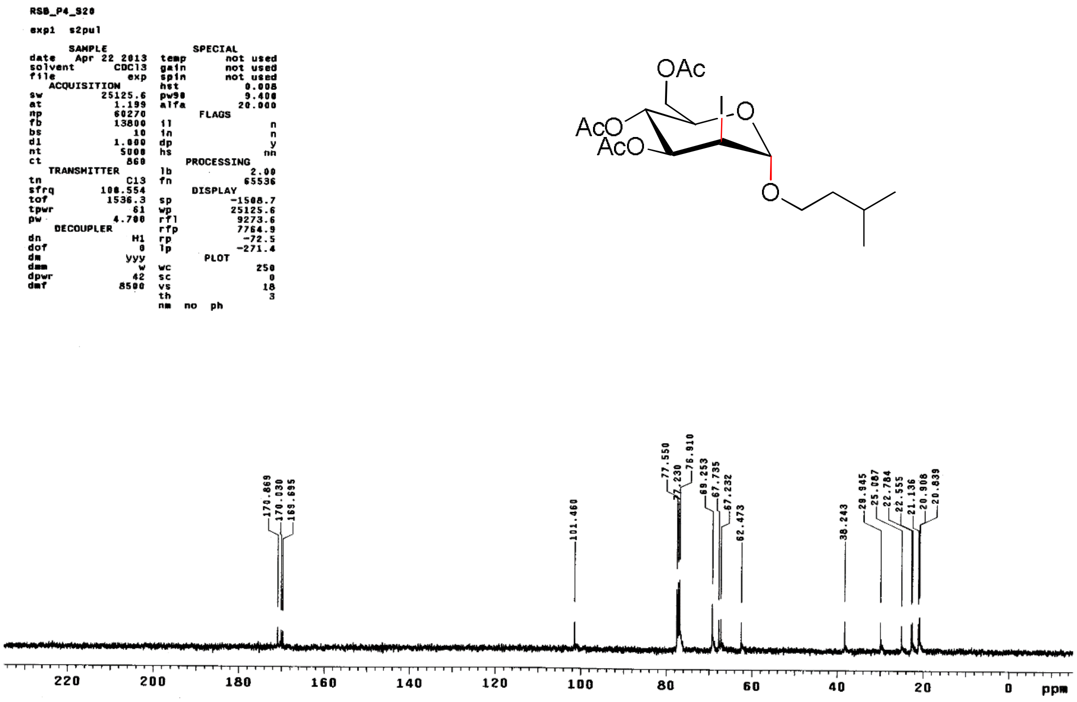
Table 4. Crystal data and structures refinement for the compound **6a** & **10**, atomic coordinates, equivalent isotropic displacement parameters and bond angles, please check the CIF.

Parameters	Compound **6a**	Compound **10**
Empirical Formula	‘$C_{15}H_{23}IO_8$’	‘$C_{30}H_{43}IO_{16}$’
Formula weight	458.23	786.54
Temperature	296 K	296 K
CCDC no	1006142	1006157
Wavelength (Å)	0.71073 Å	0.71073 Å
Crystal system	Orthorhombic	Monoclinic
Space group	P2(1)2(1)2(1)	'P 21'
Radiation type	Mo K\a	Mo K\a
Radiation source	'fine-focus sealed tube'	'fine-focus sealed tube'
a (Å)	8.4451 (2) Å	6.90610 (10) Å
b (Å)	9.2080 (2) Å	10.0119 (2) Å
c (Å)	25.7484 (6)Å	26.6266 (5) Å
α (°)	90.00°	90.00°
β (°)	90.00°	91.6930 (10)°
γ (°)	90.00°	90.00°
Cell Volume	2002.26 (8) $Å^3$	1840.24 (6) $Å^3$
Z	4	2
Density	1.527 g/cm^3	1.414 g/cm^3
F(0 0 0)	920	802
Theta range	1.58 to 28.59°	0.77 to 25.00°
Index ranges	-11<=h<=10, -12<=k<=11, -32<=l<=34	-7<=h<=8, -11<=k<=11, -31<=l<=31
Reflections collected	28963	21577
Independent reflections	5027 [R(int) = 0.0406]	6402 [R(int) = 0.0220]
Completeness to theta	28.59° 98.7 %	25.00° 99.7 %
Number of parameters	222	430
Number of restraints	0	1
Goodness-of-fit (GOF) on F^2	0.807	0.942
Refinement method	Full-matrix least-squares on F2	Full-matrix least-squares on F2

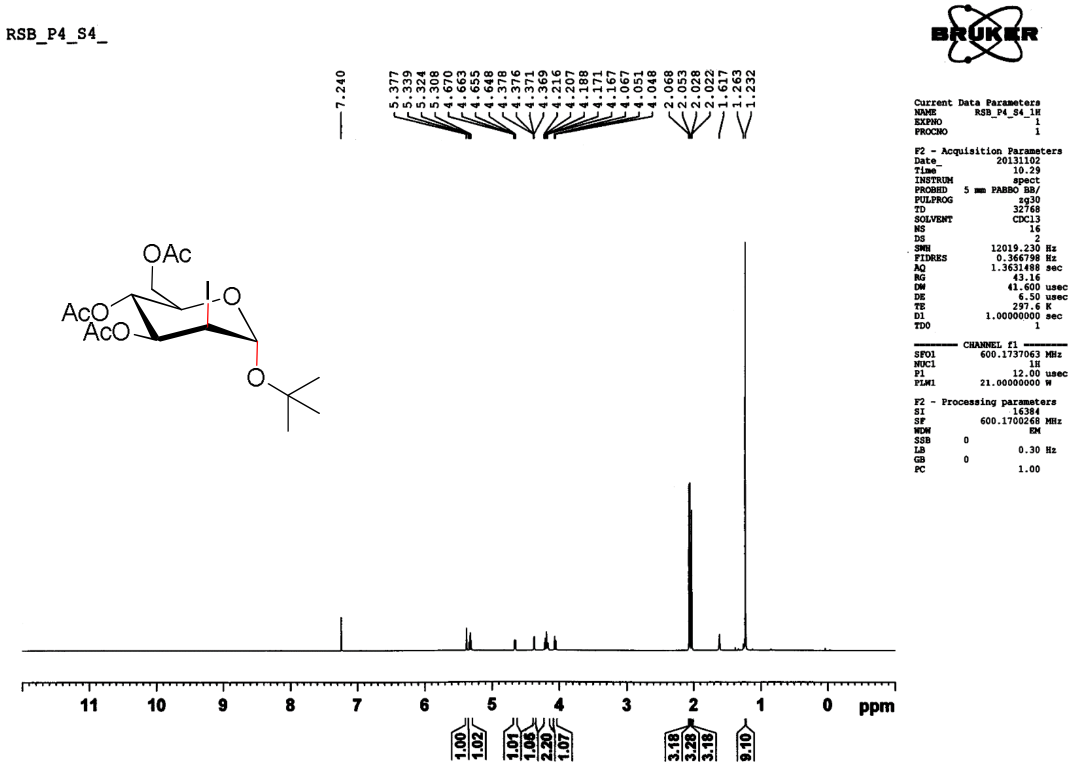
***^{1}H NMR (600 MHz, CDCl$_3$)**: Isopentyl 3,4,6-tri-O-acetyl-2-deoxy-2-iodo-D-mannopyranoside (**3c**)*



***^{13}C NMR (100 MHz, CDCl$_3$)**: Isopentyl 3,4,6-tri-O-acetyl-2-deoxy-2-iodo-D-mannopyranoside (**3c**)*



^{1}H NMR (600 MHz, CDCl$_3$):**t-Butyl 3,4,6-tri-O-acetyl-2-deoxy-2-iodo-D-mannopyranoside* ***(3j)



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DS                      2
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FIDRES           0.366798 Hz
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RG                  43.16
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DE                   6.50 usec
TE                  297.6 K
D1             1.00000000 sec
TD0                     1

======== CHANNEL f1 ========
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NUC1                   1H
P1                  12.00 usec
PLW1          21.00000000 W

F2 - Processing parameters
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SF            600.1700268 MHz
WDW                    EM
SSB       0
LB                   0.30 Hz
GB        0
PC                   1.00
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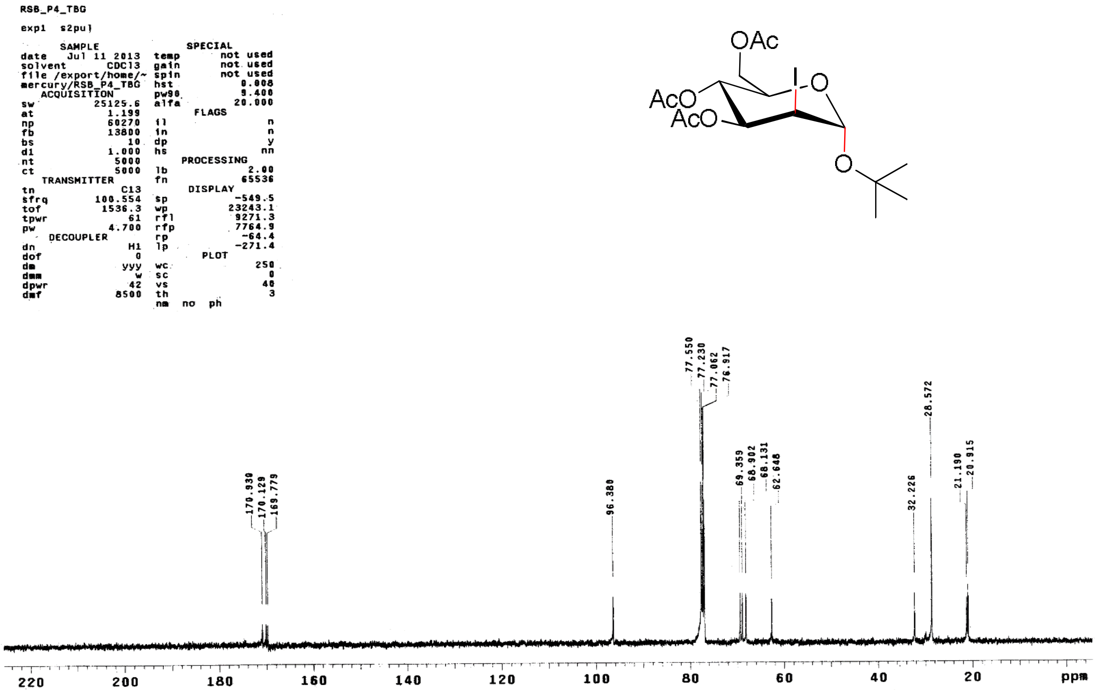
^{13}C NMR (100 MHz, CDCl$_3$)**: t-Butyl 3,4,6-tri-O-acetyl-2-deoxy-2-iodo-D-mannopyranoside* ***(3j)



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file /export/home/~   spin        not used
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   ACQUISITION        pw90           9.400
sw         25125.6    alfa          20.000
at           1.199          FLAGS
np           60270    il                 n
fb           13800    in                 n
bs              10    dp                 y
d1           1.000    hs                nn
nt            5000        PROCESSING
ct            5000    lb              2.00
   TRANSMITTER        fn             65536
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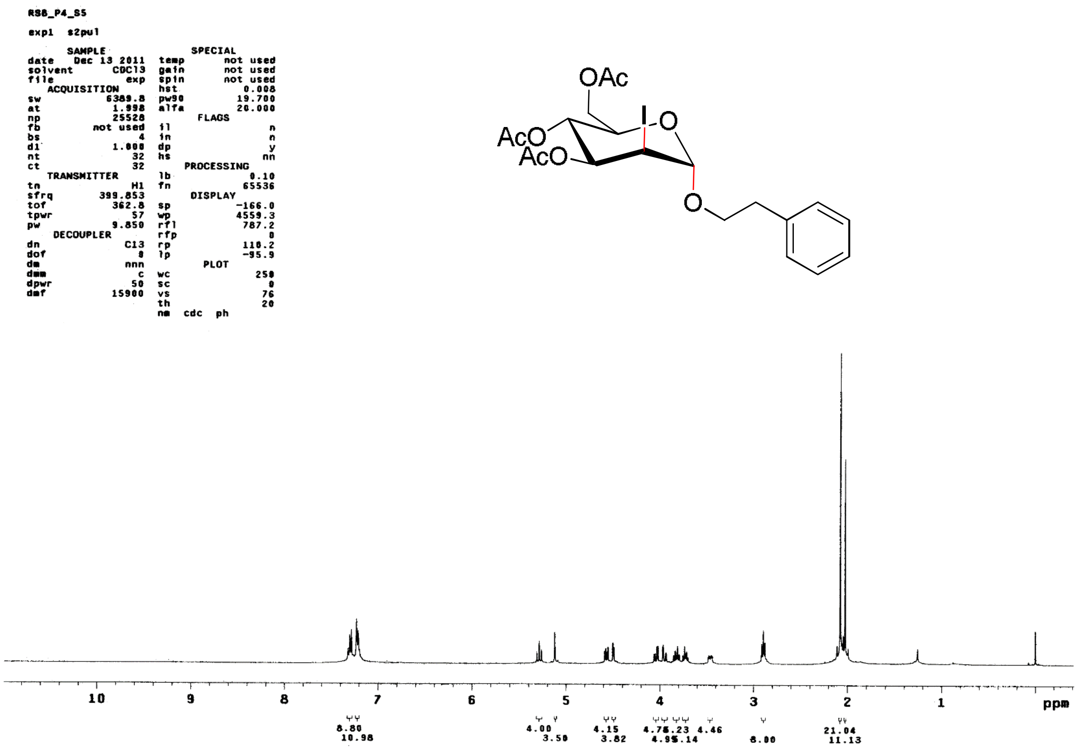
sfrq       100.554    sp            -549.5
tof         1536.3    wp           23243.1
tpwr            61    rfl           9271.3
pw           4.700    rfp           7764.9
    DECOUPLER         rp             -64.4
dn              H1    lp            -271.4
dof              0           PLOT
dm             yyy    wc               250
dmm              w    sc                 0
dpwr            42    vs                40
dmf           8500    th                 3
                      nm  no  ph
```

^{1}H NMR (400 MHz, $CDCl_3$)**: 2-Phenylethyl 3,4,6-tri-O-acetyl-2-deoxy-2-iodo-ᴅ-mannopyranoside **(3l)



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file            exp  spin       not used
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at            1.998  alfa         20.000
np            25528          FLAGS
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bs                4  in                n
d1            1.000  dp                y
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ct               32        PROCESSING
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dof               0  lp            -95.9
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dmm               c  wc              250
dpwr             50  sc                0
dmf           15900  vs               76
                     th               20
                     nm  cdc  ph
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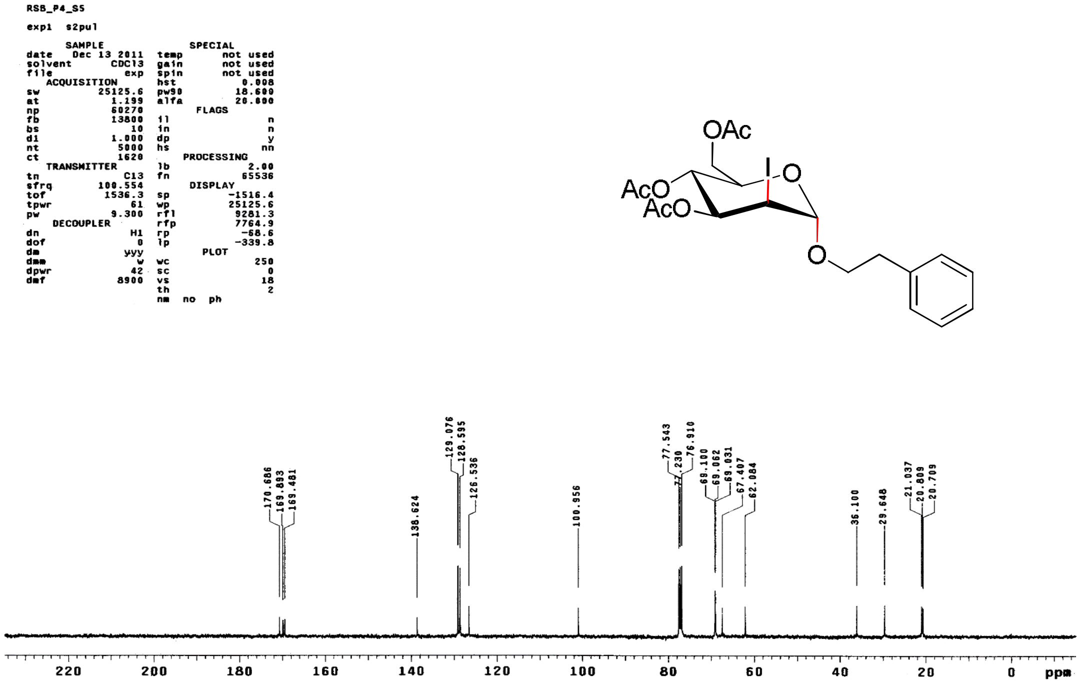
^{13}C NMR (100 MHz, $CDCl_3$)**: 2-Phenylethyl 3,4,6-tri-O-acetyl-2-deoxy-2-iodo-ᴅ-mannopyranoside **(3l)



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RSB_P4_S5

exp1  s2pul

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file            exp  spin       not used
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sw          25125.6  pw90         18.600
at            1.199  alfa         20.000
np            60270          FLAGS
fb            13800  il                n
bs               10  in                n
d1            1.000  dp                y
nt             5000  hs               nn
ct             1620        PROCESSING
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                     nm  no  ph
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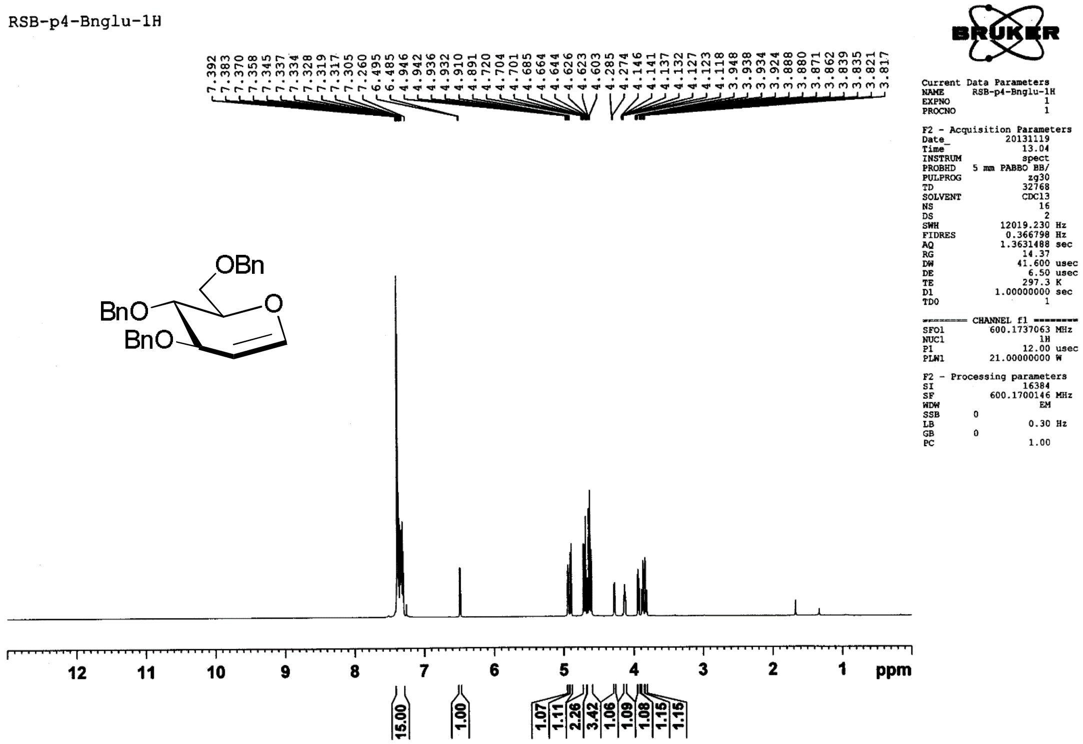
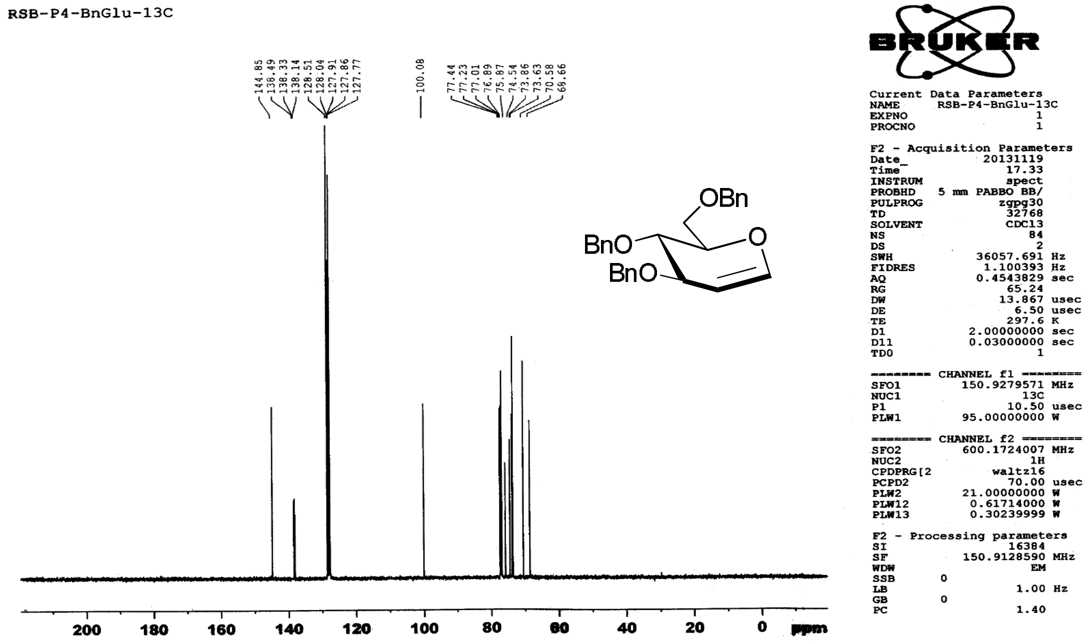
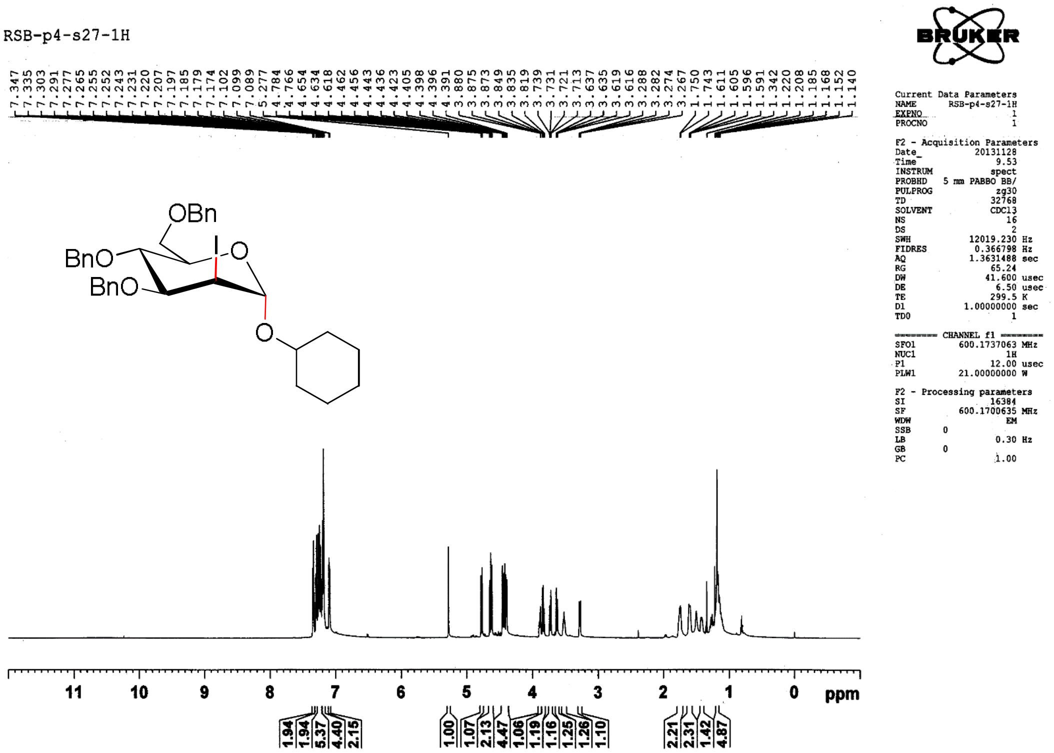
^{1}H NMR (600 MHz, CDCl$_3$)*: 3,4,6-Tri-O-benzyl-D-glucal (4)*



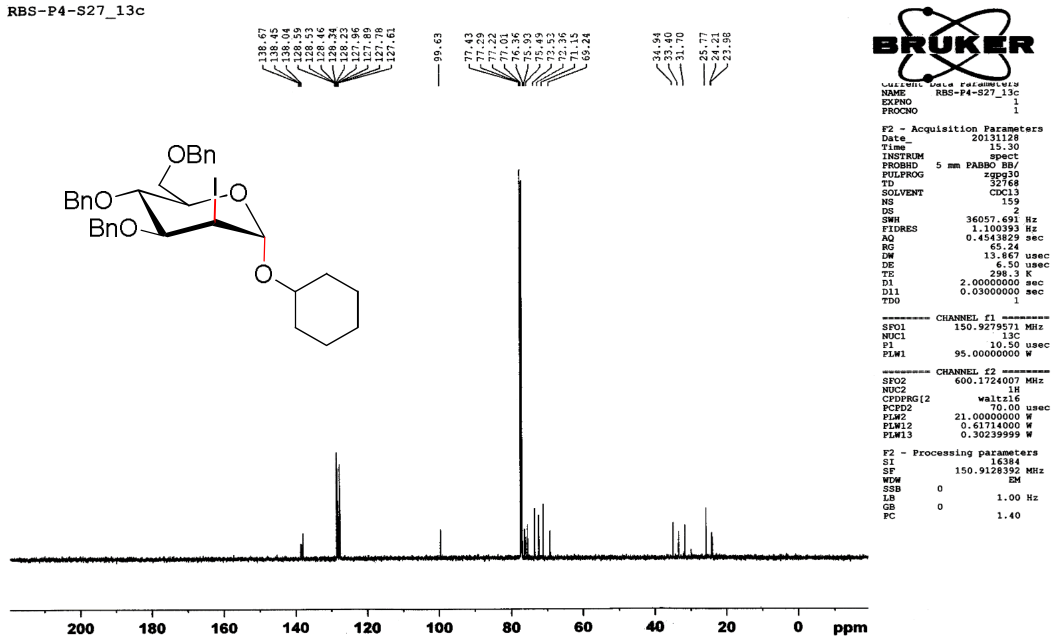
^{13}C NMR (150 MHz, CDCl$_3$)*: 3,4,6-Tri-O-benzyl-D-glucal (4)*



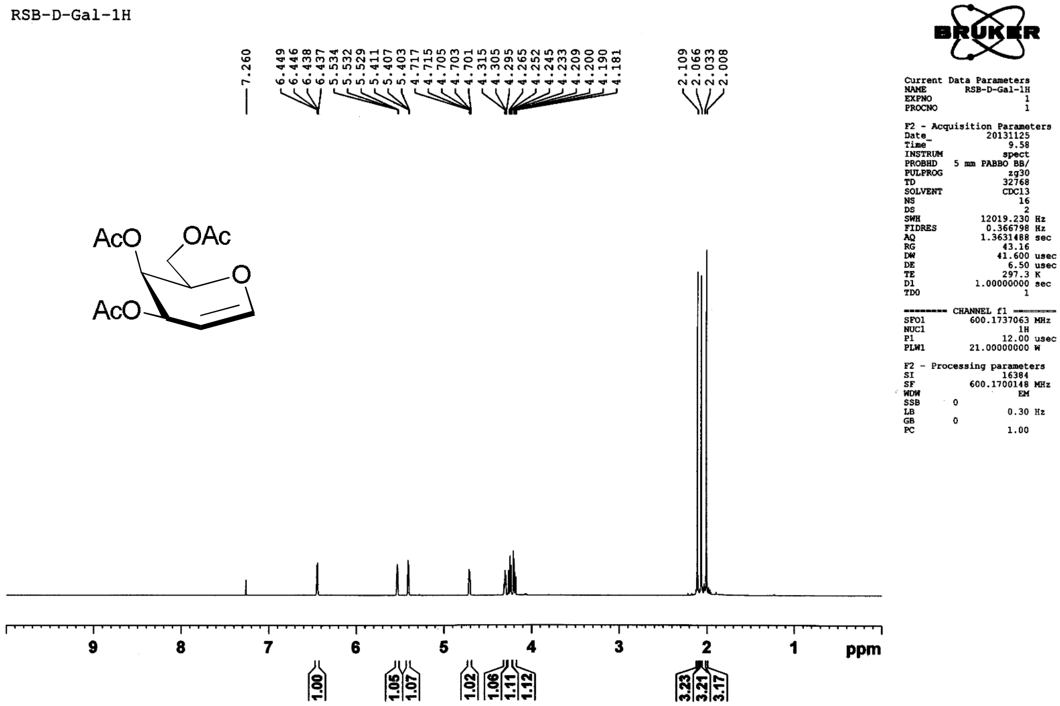
^{1}**H NMR (600 MHz, CDCl$_3$)**: *Cyclohexyl 3,4,6-tri-O-benzyl-2-deoxy-2-iodo-D-mannopyranoside (**4a**)*



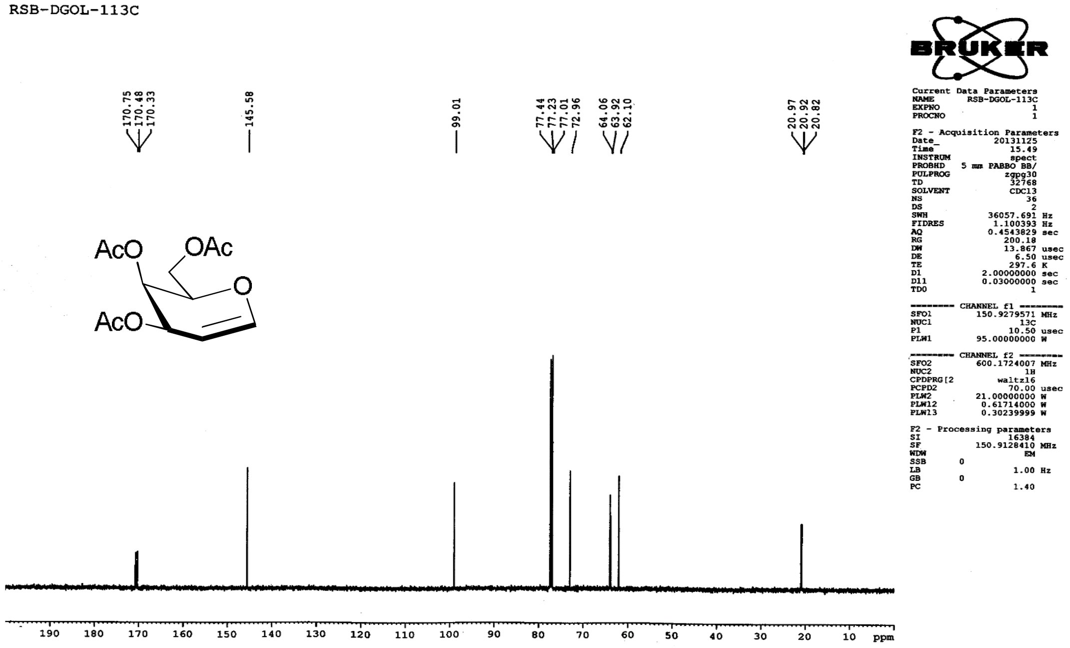
^{13}**C NMR (150 MHz, CDCl$_3$)**: *Cyclohexyl 3,4,6-tri-O-benzyl-2-deoxy-2-iodo-D-mannopyranoside (**4a**)*



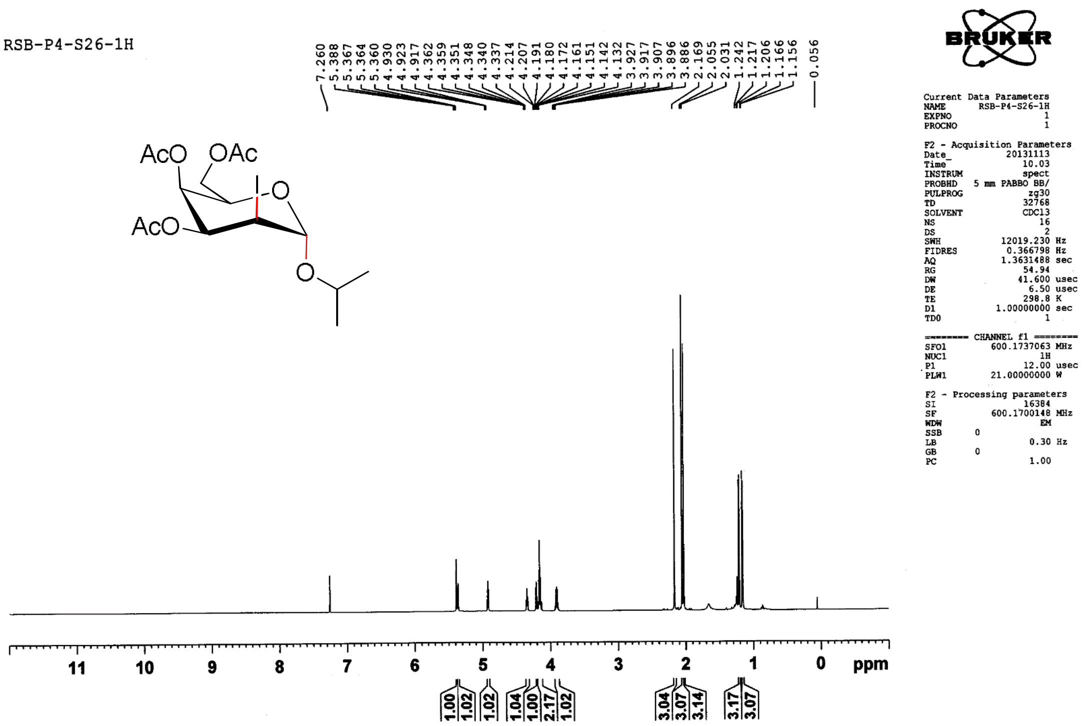
***^{1}H NMR (600 MHz, CDCl$_3$)**: 3,4,6-Tri-O-acetyl-D-galactal (**5**)*



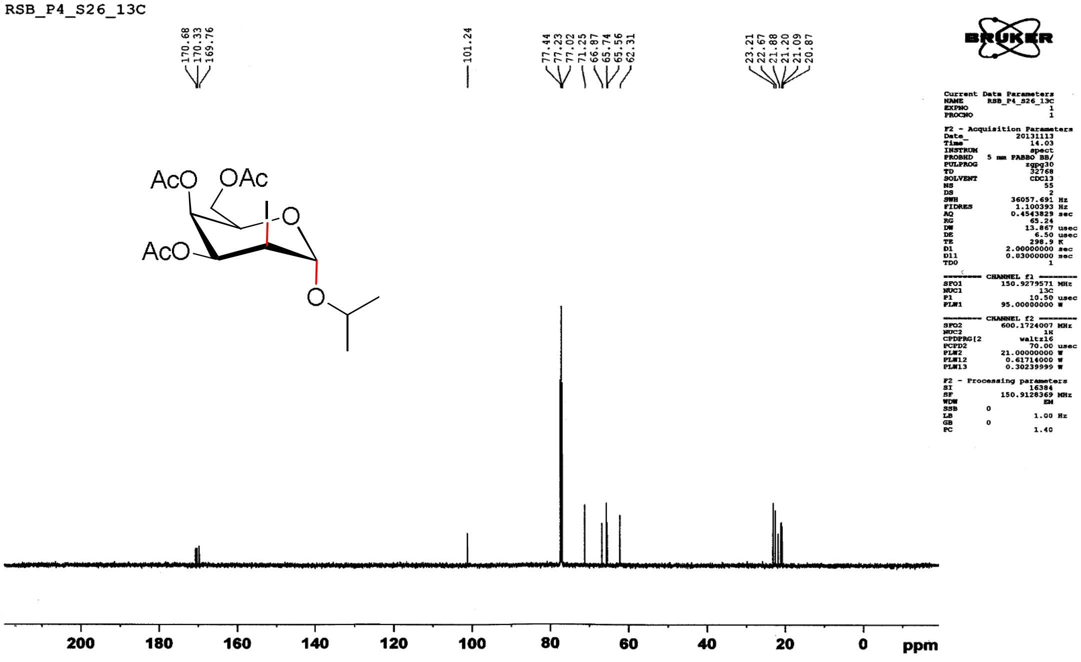
***^{13}C NMR (150 MHz, CDCl$_3$)**: 3,4,6-Tri-O-acetyl-D-galactal (**5**)*



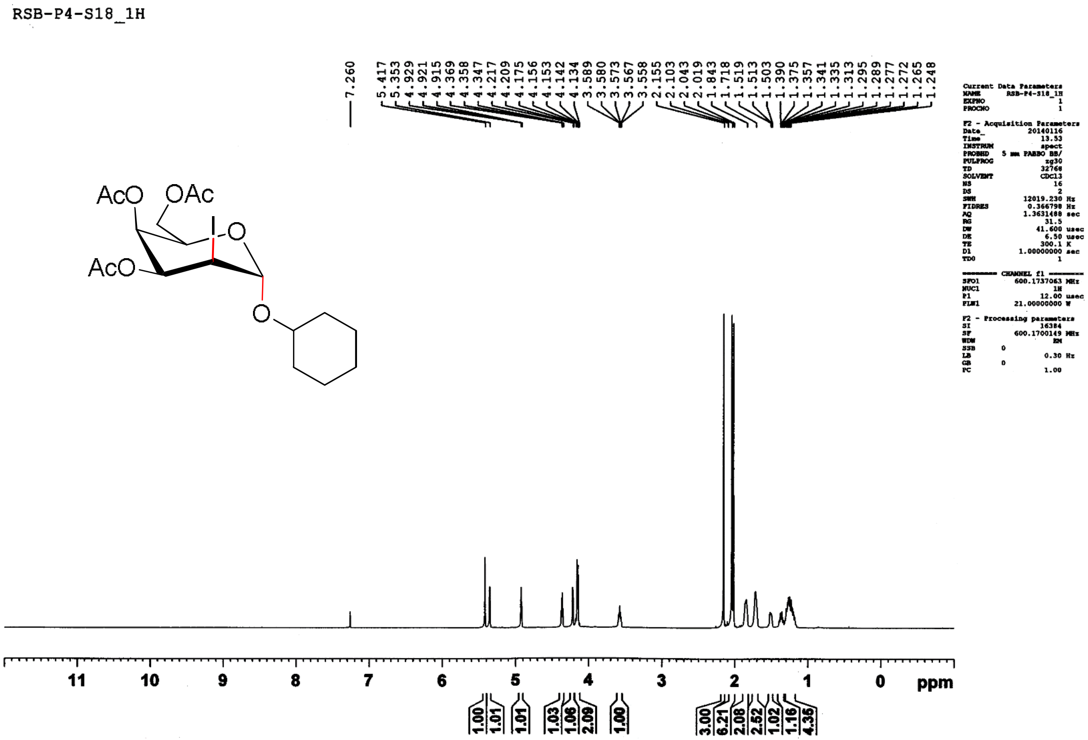
^{1}H NMR (600 MHz, CDCl$_3$): *Isopropyl 3,4,6-tri-O-acetyl-2-deoxy-2-iodo-D-talopyranoside (6a)*



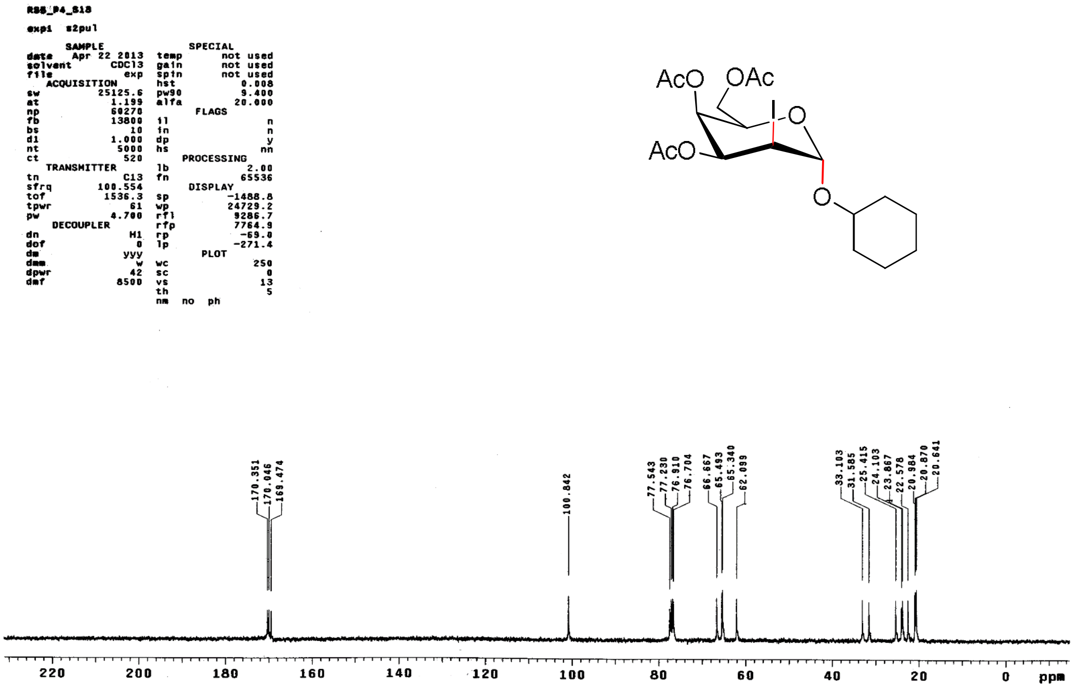
^{13}C NMR (150 MHz, CDCl$_3$): *Isopropyl 3,4,6-tri-O-acetyl-2-deoxy-2-iodo-D-talopyranoside (6a)*



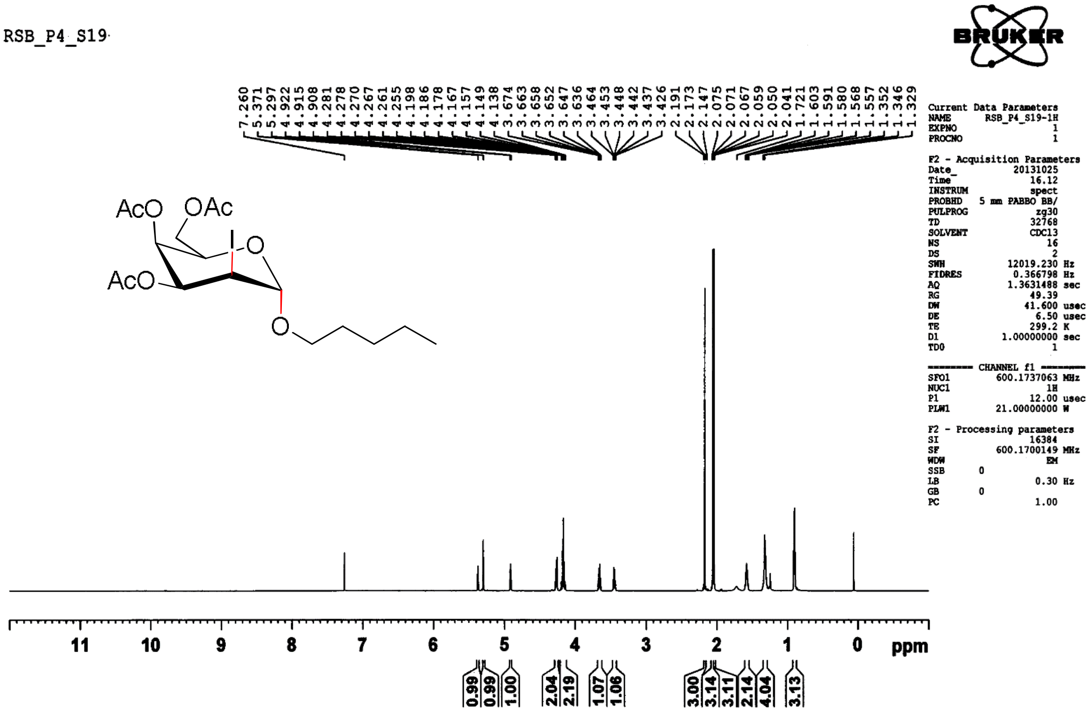
^{1}H NMR (600 MHz, CDCl$_3$)**: Cyclohexyl 3,4,6-tri-O-acetyl-2-deoxy-2-iodo-D-talopyranoside* ***(6b)



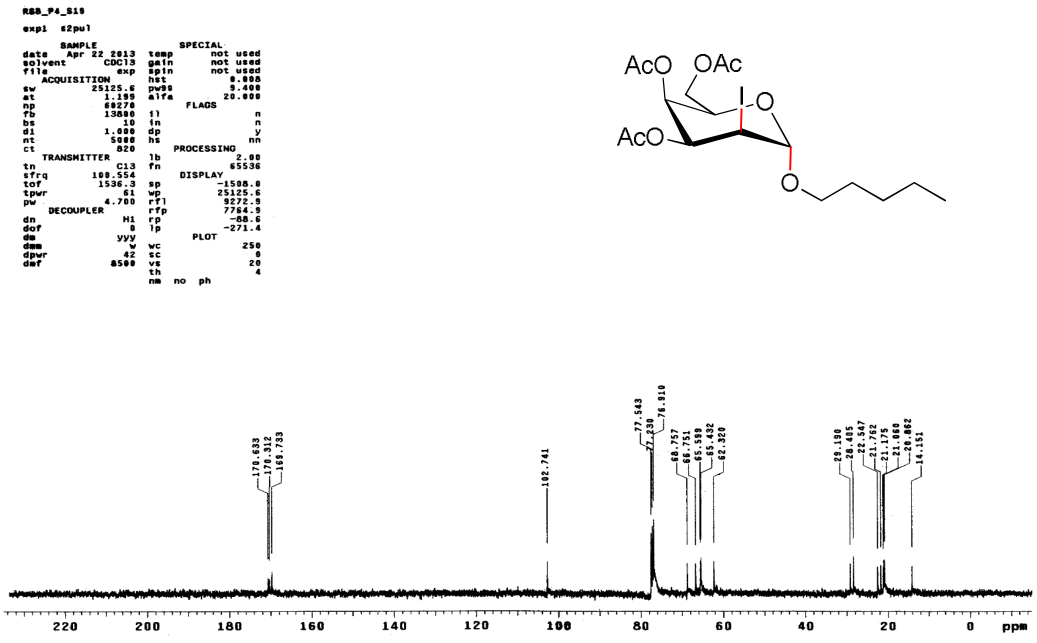
^{13}C NMR (100 MHz, CDCl$_3$)**: Cyclohexyl 3,4,6-tri-O-acetyl-2-deoxy-2-iodo-D-talopyrano side* ***(6b)



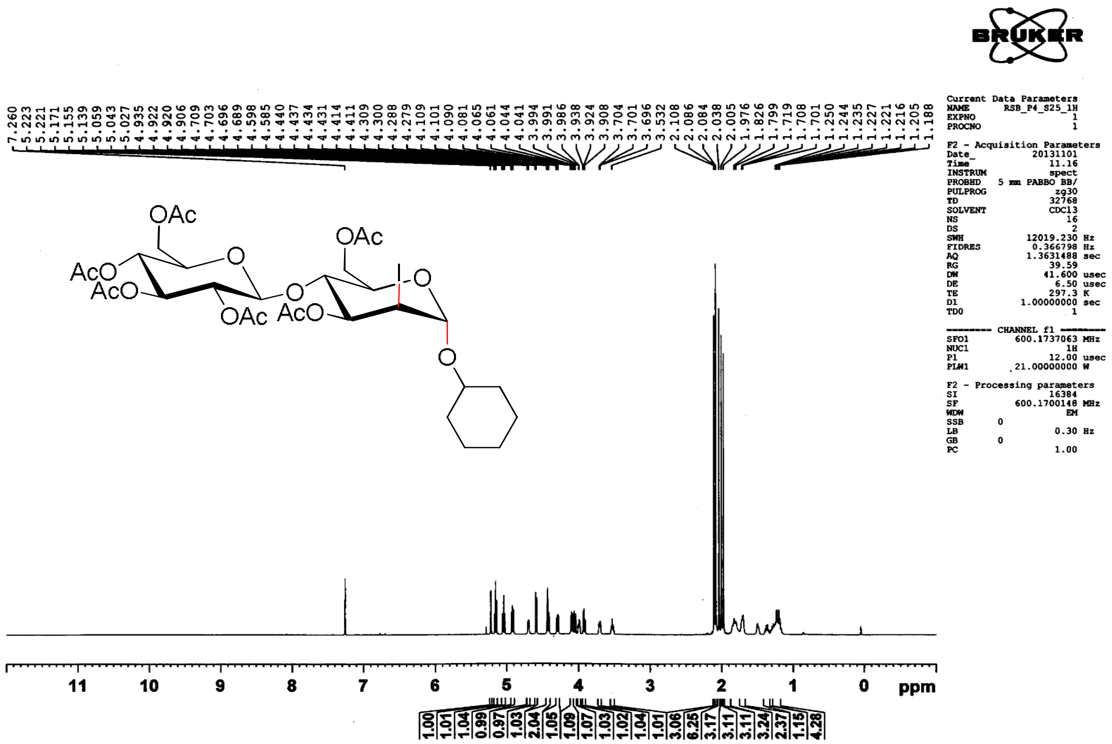
^{1}H NMR (600 MHz, $CDCl_3$)**: Pentyl 3,4,6-tri-O-acetyl-2-deoxy-2-iodo-D-talopyranoside **(6d)



^{13}C NMR (100 MHz, $CDCl_3$)**: Pentyl 3,4,6-tri-O-acetyl-2-deoxy-2-iodo-D-talopyranoside **(6d)



^{1}H NMR (600 MHz, CDCl$_3$): *Cyclohexyl 3,6-Di-O-acetyl-4-O-(2,3,4,6,-tetra-O-acetyl-β-D-glucopyranosyl)-2-deoxy-2-iodo-D-mannopyranoside* (***10***)



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PROCNO                  1

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PULPROG              zg30
TD                  32768
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DS                      2
SWH             12019.230 Hz
FIDRES           0.366798 Hz
AQ              1.3631488 sec
RG                  39.59
DW                 41.600 usec
DE                   6.50 usec
TE                  297.3 K
D1             1.00000000 sec
TD0                     1

======== CHANNEL f1 ========
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NUC1                   1H
P1                  12.00 usec
PLW1          21.00000000 W

F2 - Processing parameters
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SF            600.1700148 MHz
WDW                    EM
SSB       0
LB                   0.30 Hz
GB        0
PC                   1.00
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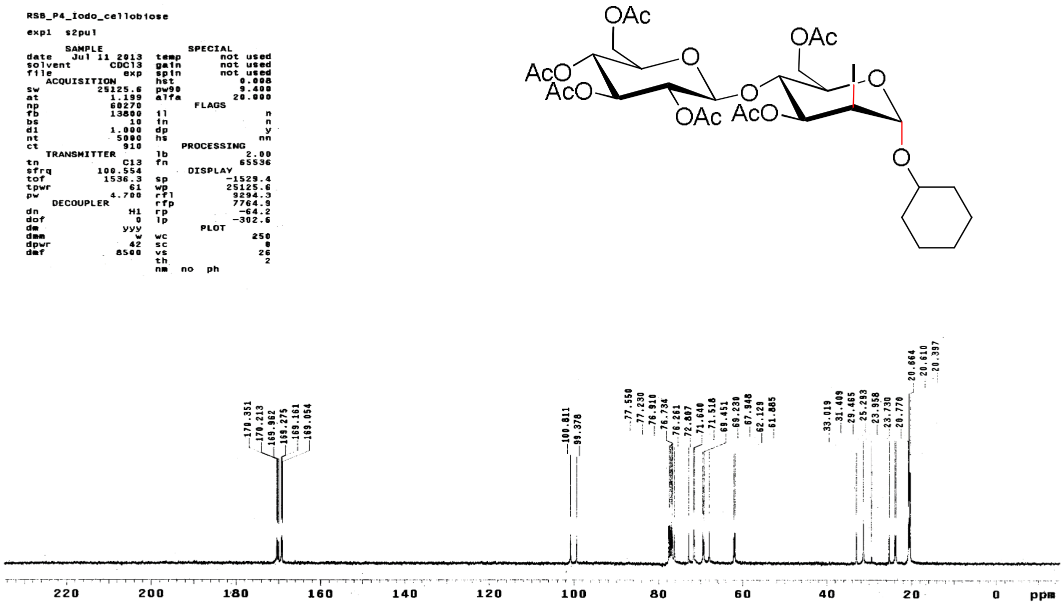
^{13}C NMR (100 MHz, CDCl$_3$): *Cyclohexyl 3,6-Di-O-acetyl-4-O-(2,3,4,6,-tetra-O-acetyl-β-D-glucopyranosyl)-2-deoxy-2-iodo-D-mannopyranoside* (***10***)



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at            1.199      alfa          20.000
np            60270           FLAGS
fb            13800      il                 n
bs               10      in                 n
d1            1.000      dp                 y
nt             5000      hs                nn
ct              910         PROCESSING
   TRANSMITTER           lb              2.00
tn              C13      fn             65536
sfrq        100.554           DISPLAY
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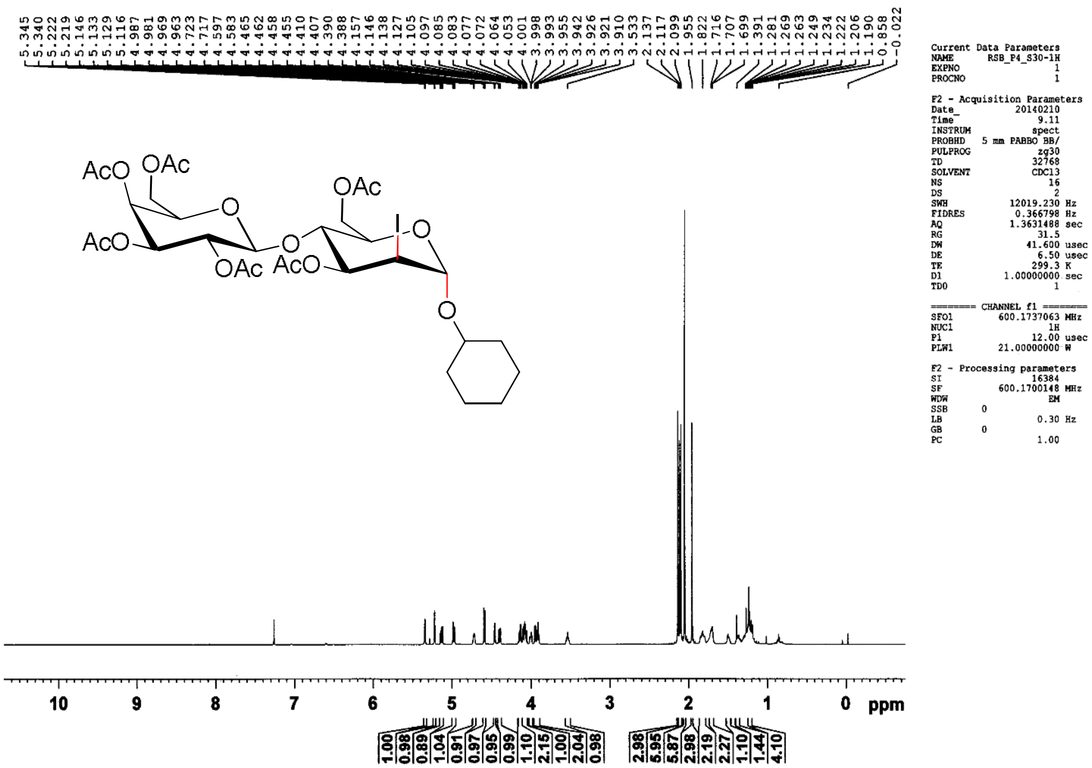
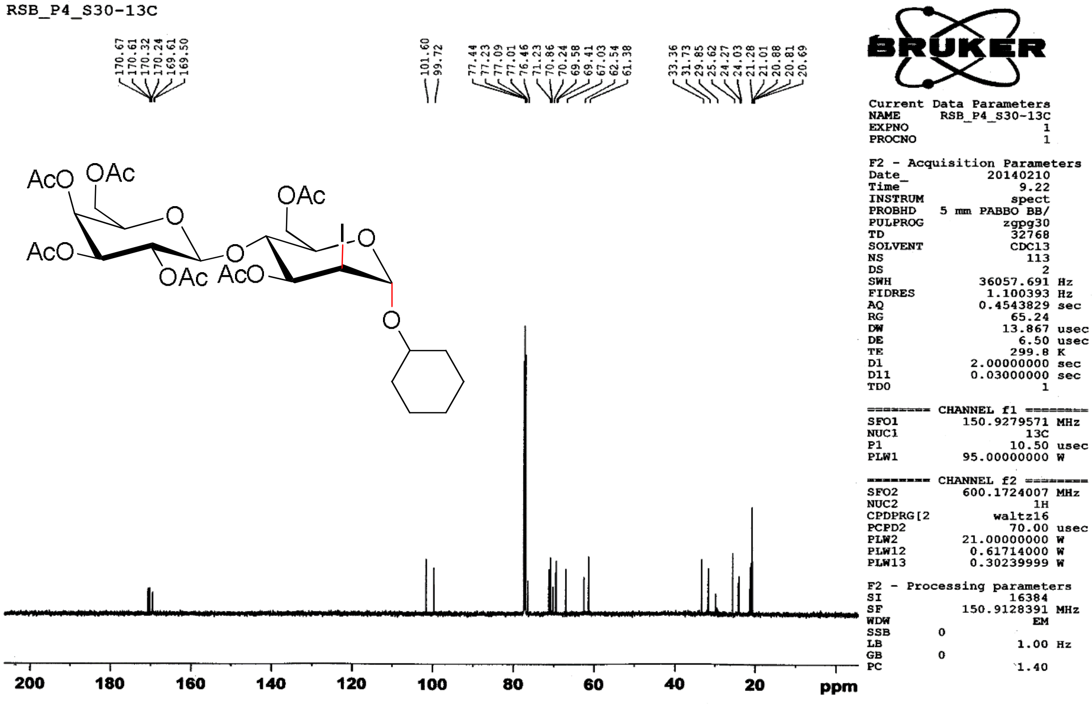
tpwr             61      wp           25125.6
pw            4.700      rfl           9294.3
    DECOUPLER            rfp           7764.9
dn               H1      rp             -64.2
dof               0      lp            -302.6
dm              yyy            PLOT
dmm               w      wc               250
dpwr             42      sc                 0
dmf            8500      vs                26
                         th                 2
                         nm  no  ph
```

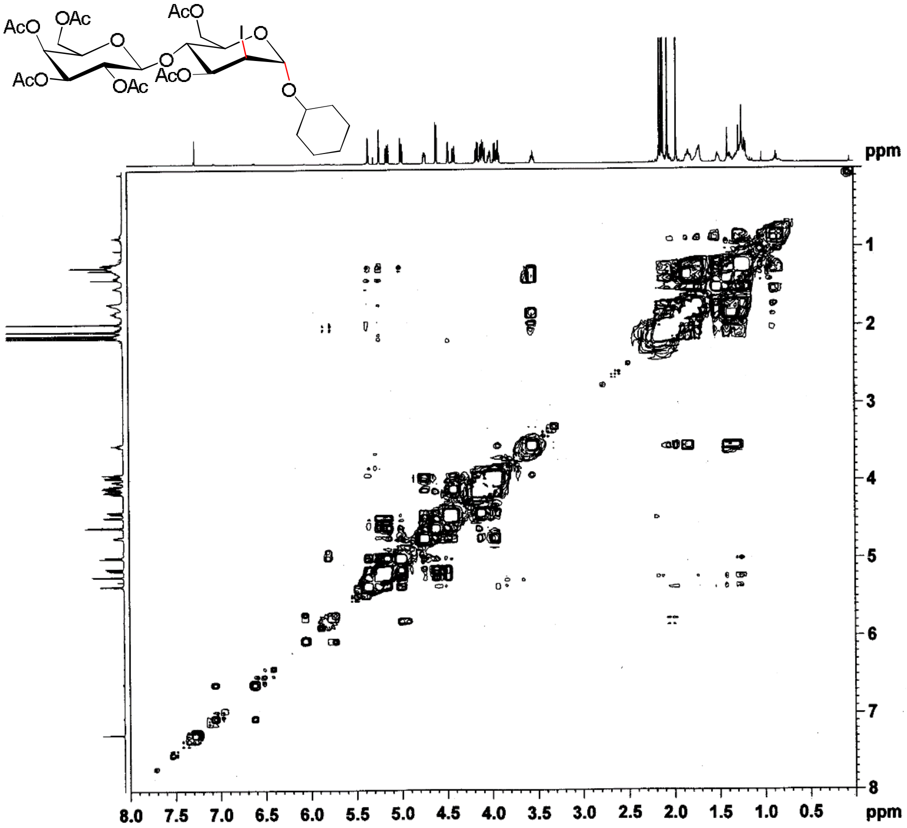
^{1}***H NMR (600 MHz, CDCl$_3$)***: *Cyclohexyl 3,6-Di-O-acetyl-4-O-(2,3,4,6,-tetra-O-acetyl-β-D-galactopyranosyl)-2-deoxy-2-iodo-D-mannopyranoside* (***15***)



^{13}***C NMR (150 MHz, CDCl$_3$)***: *Cyclohexyl 3,6-Di-O-acetyl-4-O-(2,3,4,6,-tetra-O-acetyl-β-D-galactopyranosyl)-2-deoxy-2-iodo-D-mannopyranoside* (***15***)



^{1}H-^{1}H COSY (600 MHz, CDCl$_3$): *Cyclohexyl 3,6-Di-O-acetyl-4-O-(2,3,4,6,-tetra-O-acetyl-β-D-galactopyranosyl)-2-deoxy-2-iodo-D-mannopyranoside* ***(15)***



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PROCNO                   1

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PULPROG         cosygpppqf
TD                    2048
SOLVENT              CDC13
NS                       4
DS                      16
SWH              12019.230 Hz
FIDRES            5.868765 Hz
AQ               0.0851968 sec
RG                    31.5
DW                  41.600 usec
DE                    6.50 usec
TE                   299.4 K
D0              0.00000300 sec
D1              2.00000000 sec
D11             0.03000000 sec
D12             0.00002000 sec
D13             0.00000400 sec
D16             0.00020000 sec
IN0             0.00008320 sec

======== CHANNEL f1 ========
SFO1           600.1737063 MHz
NUC1                    1H
P0                   12.00 usec
P1                   12.00 usec
P17                2500.00 usec
PLW1           21.00000000 W
PLW10           4.47340012 W

====== GRADIENT CHANNEL =====
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GPZ1                 10.00 %
P16                1000.00 usec

F1 - Acquisition parameters
TD                     118
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FIDRES          101.857887 Hz
SW                  20.026 ppm
FnMODE                  QF

F2 - Processing parameters
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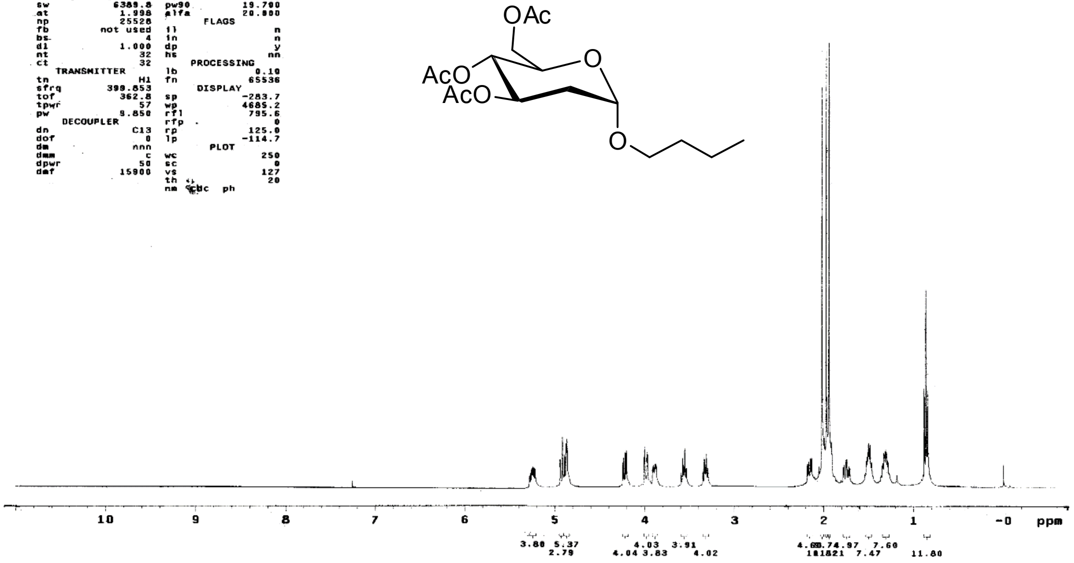
SF             600.1700000 MHz
WDW                  QSINE
SSB       0
LB        0 Hz
GB        0
PC                    1.00

F1 - Processing parameters
SI                    1024
MC2                     QF
SF             600.1700000 MHz
WDW                  QSINE
SSB       0
LB        0 Hz
GB        0
```

^{1}H NMR (400 MHz, CDCl$_3$): *Butyl 3,4,6-tri-O-acetyl-2-deoxy-D-glucopyranoside* ***(16)***



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RSB_P4_S14

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solvent        CDC13     gain       not used
file             exp     spin       not used
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sw            6389.8     pw90         19.700
at             1.998     alfa         20.000
np             25528            FLAGS
fb          not used     il                n
bs                 4     in                n
d1             1.000     dp                y
nt                32     hs               nn
ct                32          PROCESSING
   TRANSMITTER           lb             0.10
tn                H1     fn            65536
sfrq         399.853           DISPLAY
tof            362.8     sp           -283.7
tpwr              57     wp           4685.2
pw             9.850     rfl           795.6
    DECOUPLER            rfp               0
dn               C13     rp            125.0
dof                0     lp           -114.7
dm               nnn             PLOT
dmm                c     wc              250
dpwr              50     sc                0
dmf            15900     vs              127
                         th               20
                         nm  cdc   ph
```

^{13}C NMR (100 MHz, CDCl$_3$)**: Butyl 3,4,6-tri-O-acetyl-2-deoxy-D-glucopyranoside* ***(16)

```
RSB_P4_S14

exp1  s2pul

      SAMPLE              SPECIAL
date   Jun 23 2012   temp        not used
solvent      CDCl3   gain        not used
file           exp   spin        not used
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sw         25125.6   pw90          18.600
at           1.199   alfa          20.000
np           60270          FLAGS
fb           13800   il                 n
bs              10   in                 n
d1           1.000   dp                 y
nt            5000   hs                nn
ct             610        PROCESSING
    TRANSMITTER      lb              2.00
tn             C13   fn             65536
sfrq       100.554         DISPLAY
tof         1536.3   sp           -1510.3
tpwr            61   wp           25125.6
pw           9.300   rfl           9275.2
     DECOUPLER       rfp           7764.9
dn              H1   rp             -84.3
dof              0   lp            -271.4
dm             yyy            PLOT
dmm              w   wc               250
dpwr            42   sc                 0
dmf           8900   vs                17
                     th                 4
                     nm  no  ph
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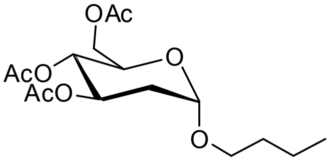
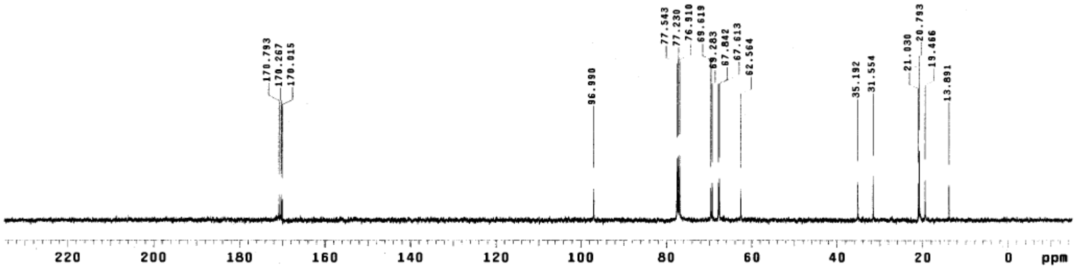




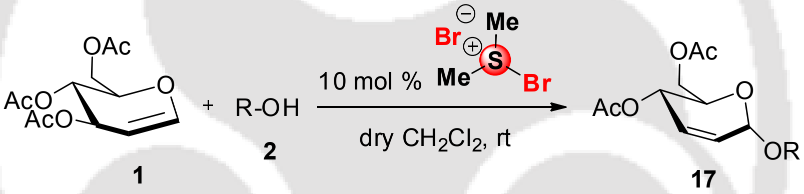
Chapter III

Bromodimethyl sulfonium bromide (BDMS) Catalyzed Synthesis of 2,3-unsaturated-O-glycosides via Ferrier rearrangement

Results and Discussion

Results and Discussion

The importance of Ferrier rearrangement on glucal and their emerging synthetic methods were discussed in Chapter I. Literature survey suggested that earlier reported methods suffered from the lack of anomeric selectivity. Thus there is a scope to develop an efficient and mild reaction conditions for the synthesis of 2,3-unsaturated-*O*-glycosides. The utilities of bromodimethylsulfonium bromide (BDMS) for various organic transformations have been demonstrated by our research group[72] as well as by others.[73] BDMS performs a crucial role as promoters[74] for glycosylation reaction. Its application in numerous synthetic transformations is also reviewed by us.[75] In this Chapter, a simple and efficient synthetic protocol was accomplished for *O*-glycosidation of 3,4,6-tri-*O*-acetyl-ᴅ-glucal via Ferrier rearrangement using bromodimethylsulfonium bromide (BDMS) as a catalyst for the synthesis of 2,3-unsaturated-*O*-glycosides, which is shown in Scheme 40.

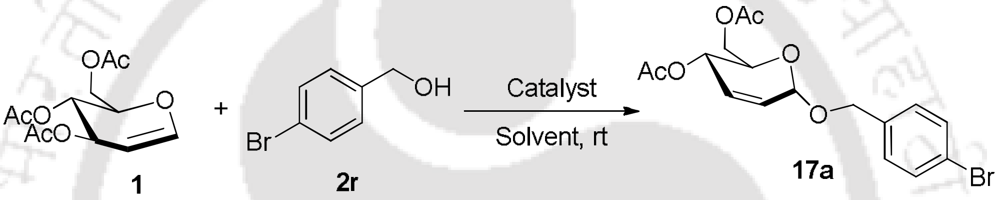


Scheme 40. Synthesis of 2,3-unsaturated-*O*-glycosides

Initial studies were performed on reaction with 3,4,6-tri-*O*-acetyl-ᴅ-glucal (**1**) and *p*-bromobenzylalchol (**2r**) as model substrates to ascertain the optimal reaction conditions. However, the reactions were scrutinized with different mol % of BDMS in dry dichloromethane (Table 5, entries 1-3) and the isolated product **17a** was characterized by ^{1}H and ^{13}C NMR spectroscopy. In addition, the reactions were performed with different solvents such as acetonitrile, dry ether and mixture of solvent system dichloromethane/acetonitrile (1:1) and their successive results are depicted in Table 5 (entries 4-6). The screening of the catalyst were also examined with metal triflates such as $Co(OTf)_2$ and $Mn(OTf)_2$ (Table 5, entries 7 and 8), which gave the required product **17a** with poor selectivity and low yield. Analyzing the obtained result revealeds that 10 mol% BDMS in dichloromethane was found to be most effective for the synthesis of 2,3-unsaturated-*O*-glycosides. It is important to note that the reaction time decreases, on increasing the catalyst amount, but there is a significant lack of increase on yield. It is also significant that the catalyst BDMS plays a vital role for high α-selectivity and good yield.

Furthermore, reaction were performed with 3,4,6-tri-*O*-acetyl-ᴅ-glucal (**1**) and benzyl alcohol (**2k**) in presence of 10 mol% BDMS under optimized reaction conditions and the expected product **17b** was obtained in 92% yield. Likewise, on reaction with a variety of alcohols such as 2-phenylethanol (**2l**), 3-phenylpropanol (**2m**), 4-phenylbutanol (**2n**) and 5-phenylpentanol (**2s**) in presence of 10 mol% catalyst under identical reaction conditions and the isolated products (**17c-f**) were obtained from 65-90% yield, which is shown in Table 6 (entries 3-6).

Table 5. Optimization of the reaction conditions[a]

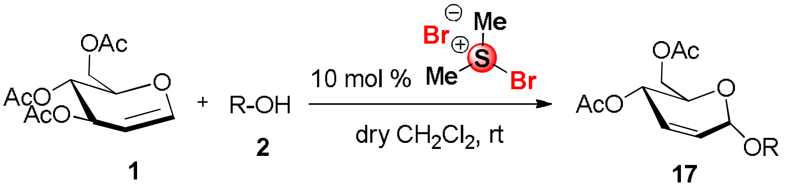


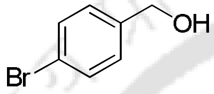
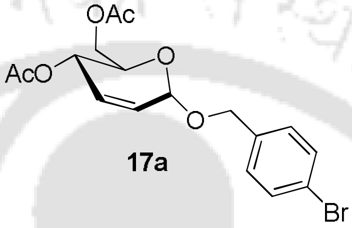
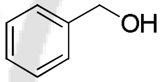
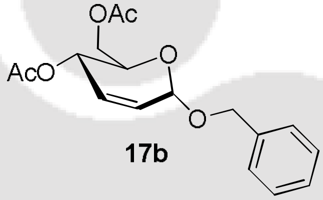
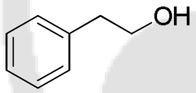
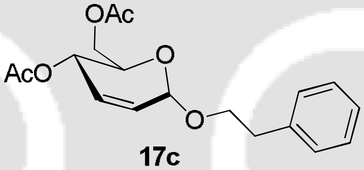
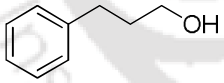
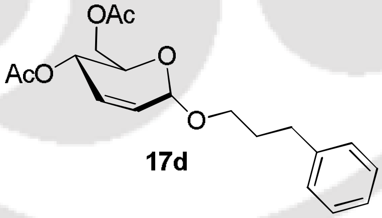
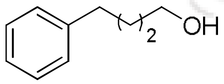
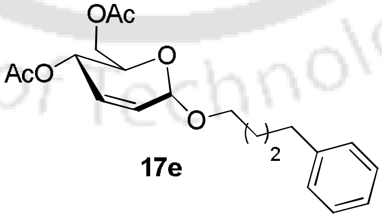
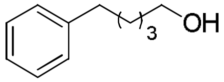
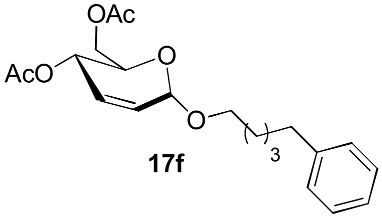
Entry	Catalyst	Solvent	Time (h)	% Yield[b] (α/β)[c]
1	5 mol% BDMS	DCM	3.5	78 (5:1)
2	10 mol% BDMS	DCM	2	85 (7:1)
3	15 mol% BDMS	DCM	1.5	83 (7:1)
4	5 mol% BDMS	CH_3CN	4	72 (5:1)
5	10 mol% BDMS	Et_2O	2.5	76 (6:1)
6	10 mol% BDMS	CH_3CN/DCM	2.5	80 (6:1)
7	5 mol% $Co(OTf)_2$	CH_3CN	6	56 (1:1)
8	5 mol% $Mn(OTf)_2$	CH_3CN	4	63 (2:1)

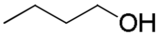
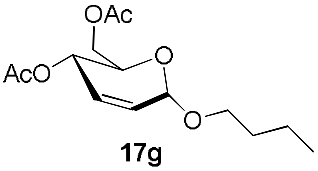
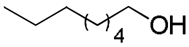
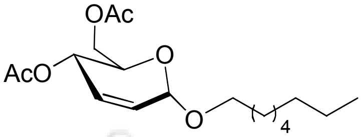
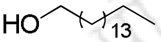
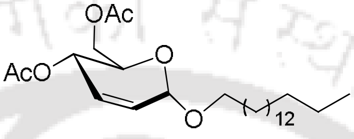
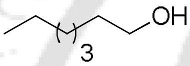
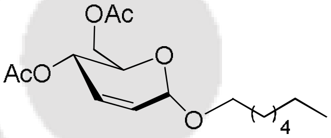
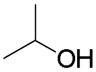
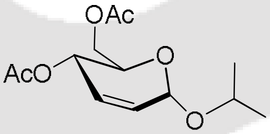
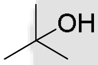
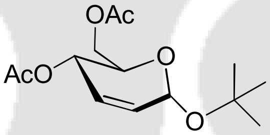
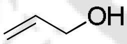
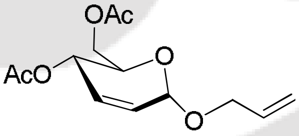
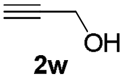
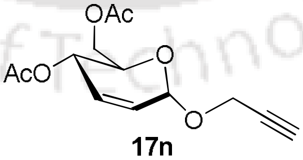
[a]All the reactions were performed using 1 mmol scale of 3,4,6-tri-*O*-acetyl-ᴅ-glucal and 1.1 *p*-bromobenzylalcohol at room temperature. [b]Isolated yield. [c]The ratio α:β was determined from the ^{1}H-NMR.

Moreover, the present protocol was further investigated with alcohols such as primary, secondary, tertiary, allylic and propargyl alcohols with 3,4,6-tri-*O*-acetyl-ᴅ-glucal (**1**) in presence of catalytic amount of BDMS under similar reaction conditions and the obtained products (**17g-n**) were isolated in good yields which is shown in Table 6 (entries 7-14).

Table 6. BDMS catalyzed Ferrier rearrangement of 3,4,6-tri-*O*-acetyl-D-glucal (**1**) with alcohol (**2**)[a]



S.No	Alcohol (**2**)	Product (**17**)	Time (h)	Yield (%)[b]	(α:β)[c]
1	 **2r**	 **17a**	2	85	7:1
2	 **2k**	 **17b**	0.5	92	8:1
3	 **2l**	 **17c**	0.5	90	9:1
4	 **2m**	 **17d**	2.5	75	12:1
5	 **2n**	 **17e**	2	72	4:1
6	 **2s**	 **17f**	3	65	3:1

7	 **2a**	 **17g**	0.5	86	6:1
8	 **2t**	 **17h**	1	78	8:1
9	 **2u**	 **17i**	2	60	α
10	 **2d**	 **17j**	1.5	62	4:1
11	 **2h**	 **17k**	1	88	10:1
12	 **2j**	 **17l**	1	85	α
13	 **2v**	 **17m**	0.5	87	18:1
14	 **2w**	 **17n**	0.5	90	α

[a] All the reactions were carried out with 1 mmol 3,4,6-tri-*O*-acetyl-D-glucal, 1.1 mmol alcohol using 10 mol% BDMS as catalyst. [b] Isolated yield. [c] The ratio (α:β) was determined by anomeric proton integration from ^{1}H-NMR.

It is noteworthy that alcohols such as cetyl alcohol (**2u**), *tert*-butyl alcohol (**2j**), propargyl alcohol (**2w**) afford only α anomer of 2,3-unsaturated-*O*-glycosides. All the isolated products were characterized through ^{1}H NMR, ^{13}C NMR, specific rotation, and elemental analysis. Furthermore, the structure of product **17n** was determined by single-crystal X-ray data, which is shown in Figure 4a.

Crystal engineering attribute significant attention in recent years due to their immense applications in drug design and molecular biology. The impact of weak interactions between the molecules leads to different arrangement of the engineered crystal motif.[76] Interestingly, the intermolecular interaction between O6….H15 in **17n** which shows prominent cavity architecture and O4…C9 & O5…H14C interactions in **17n** reflect an extensive linear network assembly which is shown in Figure 4b & 4c.

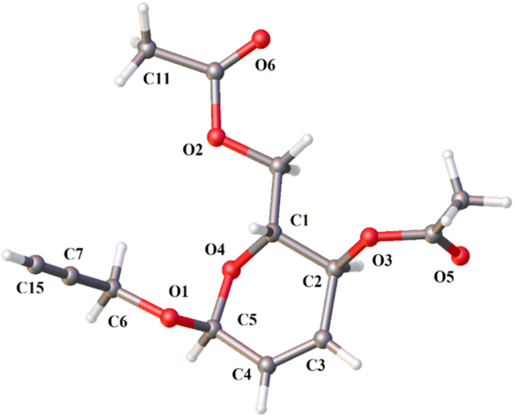


Fig 4a. X-Ray crystal structure of **17n**

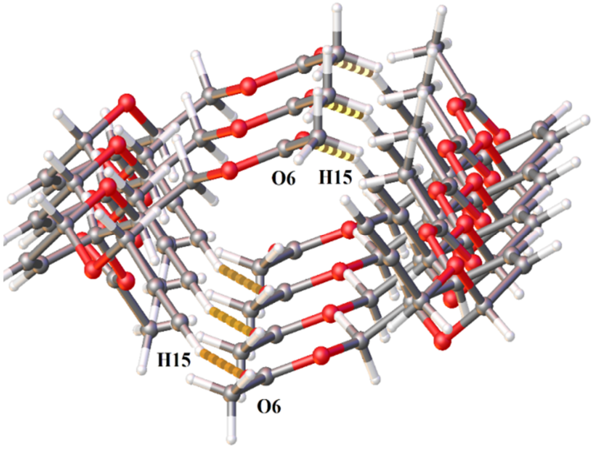


Fig 4b. O6….H15 interaction in **17n**

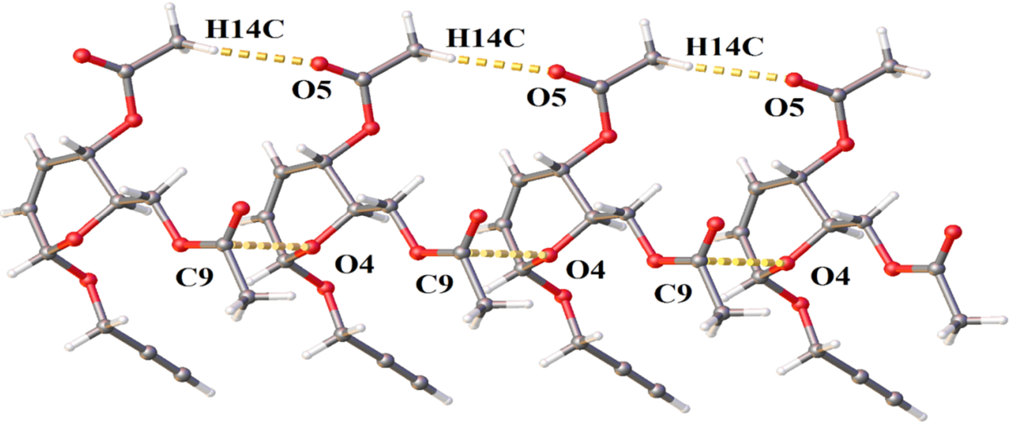
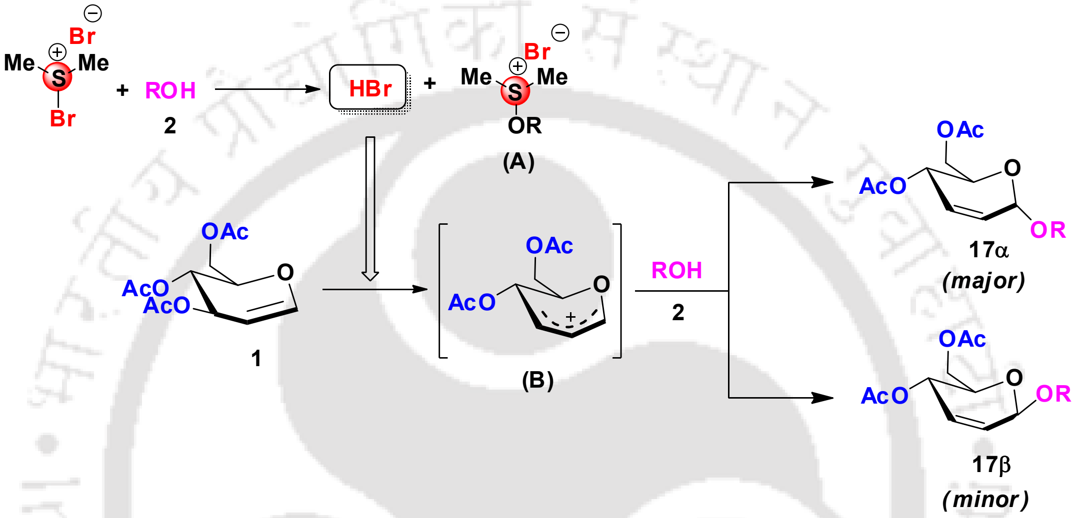


Fig 4c. O4…C9 & O5…H14C interactions in **17n**

A plausible mechanism for the formation of 2,3-unsaturated-*O*-glycoside can be described as follows: The alcohol **2** reacts with bromodimethylsulfonium bromide

(BDMS) to form the intermediate **A**, [Me$_2$S$^+$OR] Br$^-$ and dry HBr. Thus the *in situ* generated HBr which reacts with the acetyl group on C-3 position of 3,4,6-tri-*O*-acetyl-ᴅ-glucal **1** favours the formation of allylic oxocarbenium ion **B**, which was initially suggested by Ferrier. Subsequently, the alcohol **2** reacts with oxocarbenium ion **B** preferentially in a quasi-axial fashion which afford the major α-selectivity product of 2,3-unsaturated-*O*-glycosides **17α** as shown in Scheme 41.

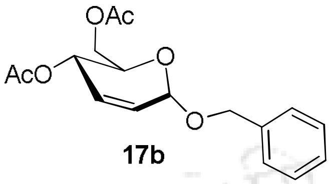
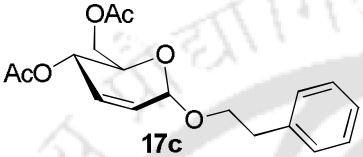
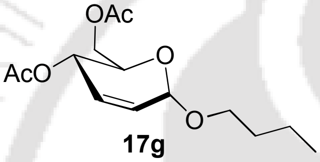
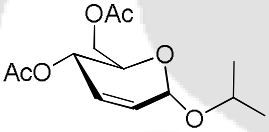
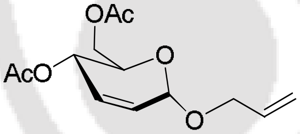
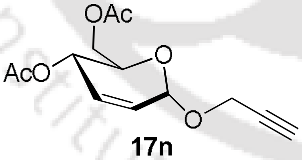


□ **Scheme 41**. Plausible mechanism for the formation of 2,3-unsaturated-*O*-glycosides

To compare the efficiency of the BDMS with aqueous HBr, a similar reaction was conducted with 3,4,6-tri-*O*-acetyl-ᴅ-glucal (**1**) and benzyl alcohol (**2k**) using 48% aqueous HBr under identical reaction condition. The output of the result shows a poor conversion of the product and the yield obtained is 30% of **17b** (based on starting material recovery).

The hydrated product is not observed while using 48% aqueous HBr. Another important aspect were a large scale reaction e.g. 10 mmol scale is carried out by using only 5 mol% catalyst. Besides that, the present protocol efficiency and generality is also compared with other recently reported method, which is shown in Table 7. The analyses of the comparative results conclude that the present protocol is equally efficient.

Table 7. Comparison of BDMS catalyzed Ferrier rearrangement with the existing reported method of 3,4,6-tri-*O*-acetyl-D-glucal with different alcohols.

S.No	Product	Catalyst used	Time (h)	Yield (%)[a]	(α:β)
1	 **17b**	BDMS $NaHSO_4$ $Fe_2(SO_4)_3.xH_2O$	0.5 5 min 1.5	92 91[60h] 85[59f]	8:1 4:1 -
2	 **17c**	BDMS H_3PO_4	0.5 15 min	90 92[57c]	9:1 8:1
3	 **17g**	BDMS $NaHSO_4$ H_3PO_4	0.5 1 10 min	86 80[60h] 93[57c]	6:1 7:1 8:1
4	 **17k**	BDMS $NbCl_5$	1 1.5 min	88 85[59e]	10:1 4:1
5	 **17m**	BDMS $NaHSO_4$ $ZnCl_2/Al_2O_3$ $NbCl_5$	0.5 5 min 20 min 2.0 min	87 72[60h] 83[60f] 95[59e]	18:1 9:1 α 4:1
6	 **17n**	BDMS $Bi(OTf)_3$ $ZnCl_2/Al_2O_3$ $NbCl_5$	0.5 5 min 10 min 2.5	90 73[58d] 88[60f] 92[59e]	α α α 4:1

[a]Isolated yield.

In summary, we have demonstrated an opportune synthetic protocol for *O*-glycosidation via Ferrier rearrangement using bromodimethylsulfonium bromide as a catalyst for the synthesis of 2,3-unsaturated-*O*-glycosides. The foremost advantages of the present methodology are: mild reaction condition, high α-selectivity, shorter reaction time, good yields and compatible with wide range of substrates. Moreover, the compound **17n** exhibit an interesting intermolecular interactions which shows a prominent cavity (O6….H15) and linear (O4…C9 & O5…H14C) supramolecular assembly.

Chapter III

Experimental Section

Bromodimethylsulfonium bromide (BDMS) Catalyzed Synthesis of 2,3-unsaturated-O-glycosides via Ferrier rearrangement

Experimental

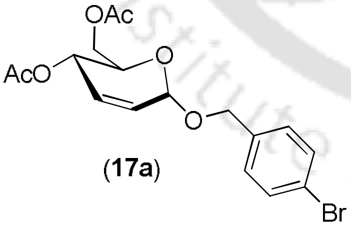
Preparation of bromodimethylsulfonium bromide (BDMS):

In a 100 mL round bottomed flask dimethyl sulfide (1.83 mL, 25 mmol) in 5 mL of dry dichloromethane was taken under ice cold condition (0-5 ^{o}C). To that bromine (25 mmol) in dry dichloromethane (5 mL) was added drop wise for a period of 10 minutes. During addition, bromodimethylsulfonium bromide began to form as light orange crystals and after complete addition of bromine, bromodimethylsulfonium bromide crystallized out, which was separated through Buchner funnel. The desired solid was washed twice with dry hexane and dried under reduced pressure and the obtained yield was 77% (4.3 g), m.p 80 ^{o}C.

General procedure for the synthesis of 2,3-unsaturated-O-glycosides

A mixture of 3,4,6-tri-*O*-acetyl-ᴅ-glucal (1 equiv.) and the corresponding alcohol (1.1 equiv.) was taken in 2 mL of dry dichloromethane. Subsequently, catalytic amount of BDMS (0.023 g) was added and stirred at room temperature and the progress of the reactions was monitored by TLC. After completion of the reaction, the solvent was evaporated under reduced pressure and the residues were subjected to column chromatography (eluted with 1:9 ethyl acetate: hexane) to get the pure product of 2,3-unsaturated-*O*-glycosides.

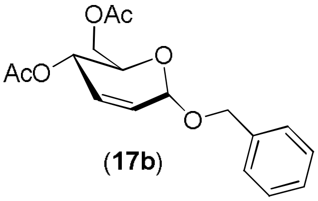
4-Bromobenzyl 4,6-di-O-acetyl-2,3-dideoxy-α-ᴅ-erythro-hex-2-enopyranoside (**17a**)



(**17a**)

$[\alpha]_D^{25}$ +47° (*c* 0.20, CH_2Cl_2); **IR** (KBr): 3456, 2924, 1742, 1488, 1369, 1231, 1069, 1038, 1010, 968, 803 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.48 (d, *J* = 8.4 Hz, 2H), 7.23 (d, *J* = 8.4 Hz, 2H), 5.91 (d, *J* = 10.4 Hz, 1H), 5.86-5.82 (m, 1H), 5.33 (dd, *J* = 10 Hz, *J* = 1.2 Hz, 1H), 5.11 (s, 1H), 4.75 (d, *J* = 12.4 Hz, 1H), 4.56-4.53 (m, 1H), 4.24 (dd, *J* = 12 Hz, *J* = 5.6 Hz, 1H), 4.16-4.10 (m, 2H), 2.09 (s, 3H), 2.08 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 170.9, 170.5, 136.8, 131.8, 129.8, 129.6, 127.7, 121.9, 93.8, 69.6, 67.3, 65.4, 63.0, 21.1, 20.9. **Anal. Calcd**. for $C_{17}H_{19}BrO_6$ (399.23): C, 51.14; H, 4.80. Found: C, 50.98; H, 4.70%.

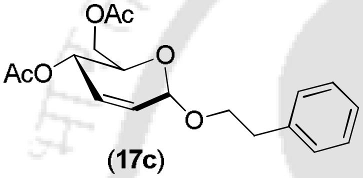
Benzyl 4,6-di-O-acetyl-2,3-dideoxy-α-D-erythro-hex-2-enopyranoside (**17b**)



(**17b**)

$[\alpha]_D^{25}$ +66° (c 0.13, CH_2Cl_2); **IR** (KBr): 3031, 2903, 1746, 1497, 1454, 1405, 1371, 1236, 1186, 1102, 1041, 969, 909, 734, 699, 605 cm^{-1}; ^{1}**H NMR** (400 MHz, $CDCl_3$): δ 7.35-7.27 (m, 5H), 5.90-5.82 (m, 2H), 5.33 (dd, J = 2.8 Hz, J = 1.6 Hz, 1H), 5.13 (s, 1H), 4.80 (d, J = 11.6 Hz, 1H), 4.62-4.57 (m, 1H), 4.30-4.22 (m, 1H), 4.17-4.08 (m, 2H), 2.08 (s, 3H), 2.06 (s, 3H); ^{13}**C NMR** (100 MHz, $CDCl_3$): δ 170.7, 170.2, 137.6, 129.3, 128.4, 128.0, 127.8, 127.7, 93.6, 70.2, 67.0, 65.2, 62.9, 20.9, 20.7. **Anal. Calcd**. for $C_{17}H_{20}O_6$ (320.33): C, 63.74; H, 6.29. Found: C, 63.50; H, 6.21%.

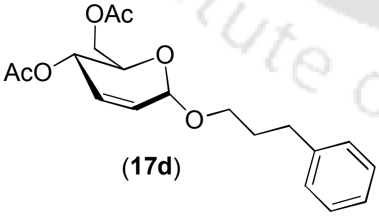
2-Phenylethyl 4,6-di-O-acetyl-2,3-dideoxy-α-D-erythro-hex-2-enopyranoside (**17c**)



(**17c**)

$[\alpha]_D^{25}$ +76° (c 0.16, CH_2Cl_2); **IR** (KBr): 3028, 2928, 1743, 1496, 1370, 1228, 1105, 1039, 972, 909, 751, 700, 669 cm^{-1}; ^{1}**H NMR** (400 MHz, $CDCl_3$): δ 7.23-7.18 (m, 2H), 7.16-7.12 (m, 3H), 5.81 (dd, J = 11.6 Hz, J = 11.2 Hz, 1H), 5.75-5.71 (m, 1H), 5.21 (dd, J = 9.6 Hz, J = 1.6 Hz, 1H), 4.94 (s, 1H), 4.10 (dd, J = 12 Hz, J = 5.2 Hz, 1H), 3.96 (dd, J = 12 Hz, J = 2.8 Hz, 1H), 3.92-3.86 (m, 2H), 3.71-3.66 (m, 1H), 2.86 (t, 2H), 2.0 (s, 3H), 1.99 (s, 3H); ^{13}**C NMR** (100 MHz, $CDCl_3$): δ 170.9, 170.4, 138.9, 129.2, 129.0, 128.5, 127.8, 126.4, 94.5, 69.6, 67.0, 65.3, 63.0, 36.4, 21.1, 20.9. **Anal. Calcd**. for $C_{18}H_{22}O_6$ (334.36): C, 64.66; H, 6.63. Found: C, 64.50; H, 6.51%.

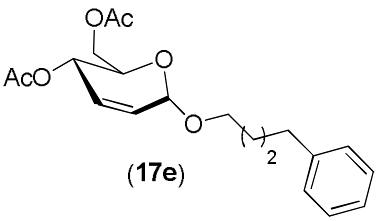
3-Phenylpropanyl 4,6-di-O-acetyl-2,3-dideoxy-α-D-erythro-hex-2-enopyranoside (**17d**)



(**17d**)

$[\alpha]_D^{25}$ +81° (c 0.28, CH_2Cl_2); **IR** (KBr): 3060, 3026, 2942, 1744, 1603, 1496, 1453, 1370, 1235, 1106, 1038, 978, 909, 746, 700, 605 cm^{-1}; ^{1}**H NMR** (400 MHz, $CDCl_3$): δ 7.22-7.07 (m, 5H), 5.81 (d, J = 10.4 Hz, 1H), 5.78-5.74 (m, 1H), 5.23 (dd, J = 9.2 Hz, J = 1.6 Hz, 1H), 4.93 (s, 1H), 4.18-4.14 (m, 1H), 4.08-4.01 (m, 2H), 3.75-3.69 (m, 1H), 3.47-3.41 (m, 1H), 2.67-2.57 (m, 2H), 2.0 (s, 3H), 1.96 (s, 3H), 1.89-1.85 (m, 2H); ^{13}**C NMR** (100 MHz, $CDCl_3$): δ 170.8, 170.3, 141.7, 129.1, 128.5, 128.0, 125.9, 94.6, 68.2, 67.0, 65.3, 63.0, 32.5, 31.3, 21.0, 20.8. **Anal. Calcd**. for $C_{19}H_{24}O_6$ (348.39): C, 65.50; H, 6.94. Found: C, 65.40; H, 6.82%.

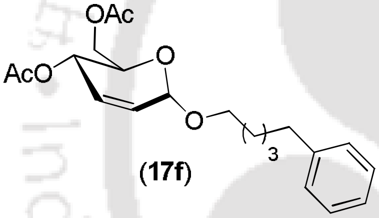
4-Phenyl butanyl 4,6-di-O-acetyl-2,3-dideoxy-α-D-erythro-hex-2-enopyranoside (**17e**)



(**17e**)

$[\alpha]_D^{25}$ +54° (*c* 0.22, CH_2Cl_2); **IR** (KBr): 3026, 2936, 2861, 1744, 1496, 1453, 1370, 1233, 1041, 748, 699, 669 cm^{-1}; ^{1}**H NMR** (400 MHz, $CDCl_3$): δ 7.29-7.13 (m, 5H), 5.87 (d, *J* = 11.6 Hz, 1H), 5.83-5.81 (m, 1H), 5.30 (dd, *J* = 9.6 Hz, *J* = 1.2 Hz, 1H), 5.0 (s, 1H), 4.25-4.19 (m, 1H), 4.15 (dd, *J* = 12 Hz, *J* = 2 Hz, 1H), 4.10-4.06 (m, 1H), 3.82-3.76 (m, 1H), 3.54-3.47 (m, 1H), 2.67-2.59 (m, 2H), 2.07 (s, 3H), 2.06 (s, 3H), 1.72-1.62 (m, 4H); ^{13}**C NMR** (100 MHz, $CDCl_3$): δ 170.8, 170.3, 142.3, 129.0, 128.5, 128.4, 128.0, 125.8, 94.5, 68.8, 66.9, 65.3, 63.1, 35.7, 29.4, 28.2, 21.0, 20.8. **Anal. Calcd**. for $C_{20}H_{26}O_6$ (362.41): C, 66.28; H, 7.23. Found: C, 66.15; H, 7.14%.

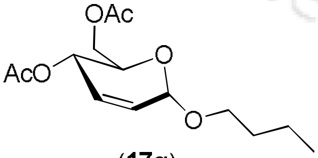
5-Phenyl pentyl 4,6-di-O-acetyl-2,3-dideoxy-α-D-erythro-hex-2-enopyranoside (**17f**)



(**17f**)

$[\alpha]_D^{25}$ +12.8° (*c* 0.40, CH_2Cl_2); **IR** (KBr): 3061, 3025, 2934, 2858, 1748, 1495, 1453, 1367, 1228, 1120, 1046, 907, 748, 700, 601 cm^{-1}; ^{1}**H NMR** (400 MHz, $CDCl_3$): δ 7.28-7.23 (m, 2H), 7.17-7.15 (m, 3H), 5.94-5.83 (m, 2H), 5.30 (d, *J* = 9.2 Hz, 1H), 5.0 (s, 1H), 4.22-4.17 (m, 1H), 4.03-3.99 (m, 1H), 3.87-3.73 (m, 1H), 3.52-3.44 (m, 2H), 2.63-2.59 (m, 2H), 2.07 (s, 3H), 2.06 (s, 3H), 1.66-1.62 (m, 4H), 1.44-1.39 (m, 2H); ^{13}**C NMR** (100 MHz, $CDCl_3$): 171.0, 170.5, 142.7, 129.2, 128.5, 128.1, 126.3, 125.9, 94.6, 69.0, 67.0, 65.5, 63.2, 36.0, 31.4, 29.8, 26.1, 21.2, 21.0. **Anal. Calcd**. for $C_{21}H_{28}O_6$ (376.44): C, 67.00; H, 7.50. Found: C, 66.85; H, 7.40%.

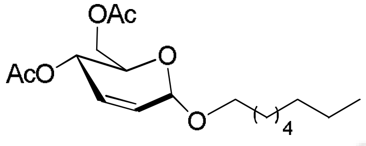
n-Butyl 4,6-di-O-acetyl-2,3-dideoxy-α-D-erythro-hex-2-enopyranoside (**17g**)



(**17g**)

$[\alpha]_D^{25}$ +106° (*c* 0.23, CH_2Cl_2); **IR** (KBr): 2959, 2934, 2873, 1746, 1371, 1233, 1105, 1043, 907, 732, 605 cm^{-1}; ^{1}**H NMR** (400 MHz, $CDCl_3$): δ 5.82-5.75 (m, 1H), 5.72-5.67 (m, 1H), 5.16 (dd, *J* = 9.6 Hz, *J* = 1.2 Hz, 1H), 4.88 (s, 1H), 4.10 (dd, *J* = 12.4 Hz, *J* = 5.6 Hz, 1H), 4.0 (dd, *J* = 12 Hz, *J* = 2.4 Hz, 1H), 3.98-3.94 (m, 1H), 3.68-3.61 (m, 1H), 3.40-3.33 (m, 1H), 1.95 (s, 3H), 1.94 (s, 3H), 1.48-1.41 (m, 2H), 1.29-1.22 (m, 2H), 0.79 (t, 3H); ^{13}**C NMR** (100 MHz, $CDCl_3$): δ 170.6, 170.2, 128.9, 127.9, 94.3, 68.5, 66.8, 65.2, 63.0, 31.7, 20.8, 20.7, 19.3, 13.7. **Anal. Calcd**. for $C_{14}H_{22}O_6$ (286.32): C, 58.73; H, 7.74. Found: C, 58.50; H, 7.65%.

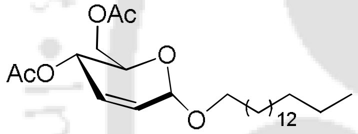
Octyl 4,6-di-O-acetyl-2,3-dideoxy-α-ᴅ-erythro-hex-2-enopyranoside (**17h**)



(17h)

$[\alpha]_D^{25}$ +16.6° (*c* 0.62, CH_2Cl_2); **IR** (KBr): 3060, 3025, 2933, 2858, 1748, 1602, 1494, 1453, 1370, 1230, 1120, 1047, 906, 746, 700 cm^{-1}; ^{1}**H NMR** (400 MHz, $CDCl_3$): δ 5.95-5.89 (m, 1H), 5.87-5.85 (m, 1H), 5.31 (d, *J* = 9.6 Hz, 1H), 5.03 (s, 1H), 4.28-4.22 (m, 1H), 4.19-4.16 (m, 1H), 4.13-4.09 (m, 1H), 3.80-3.74 (m, 1H), 3.53-3.46 (m, 1H), 2.10 (s, 3H), 2.08 (s, 3H), 1.63-1.57 (m, 5H), 1.32-1.29 (m, 7H), 0.87 (t, *J* = 5.6 Hz, 3H); ^{13}**C NMR** (100 MHz, $CDCl_3$): δ 170.5, 170.4, 129.0, 128.1, 94.5, 69.1, 67.0, 65.4, 63.1, 31.9, 29.8, 29.5, 29.4, 26.3, 22.7, 21.0, 20.9, 14.2. **Anal. Calcd**. for $C_{18}H_{30}O_6$ (342.42): C, 63.14; H, 8.83. Found: C, 62.95; H, 8.70%.

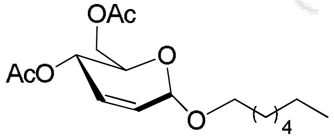
Hexadecyl 4,6-di-O-acetyl-2,3-dideoxy-α-ᴅ-erythro-hex-2-enopyranoside (**17i**)



(17i)

$[\alpha]_D^{25}$ +50° (*c* 0.07, CH_2Cl_2); **IR** (KBr): 2924, 2853, 1748, 1466, 1369, 1233, 1105, 1040 cm^{-1}; ^{1}**H NMR** (400 MHz, $CDCl_3$): δ 5.88 (d, *J* = 10.4 Hz, 1H), 5.85-5.82 (m, 1H), 5.31 (dd, *J* = 10 Hz, *J* = 1.2 Hz, 1H), 5.02 (s, 1H), 4.25 (dd, *J* = 12 Hz, *J* = 5.2 Hz, 1H), 4.17 (dd, *J* = 12 Hz, *J* = 2.4 Hz, 1H), 4.12-4.09 (m, 1H), 3.78-3.73 (m, 1H), 3.53-3.47 (m, 1H), 2.10 (s, 3H), 2.08 (s, 3H), 1.63-1.59 (m, 4H), 1.25-1.20 (m, 24H), 0.88 (t, *J* = 6.34, 3H); ^{13}**C NMR** (100 MHz, $CDCl_3$): δ 170.8, 170.3, 129.2, 128.1, 94.6, 69.2, 67.0, 65.5, 63.3, 32.1, 29.8 (9C), 29.6, 26.4, 22.9, 21.2, 21.0, 14.3. **Anal. Calcd**. for $C_{26}H_{46}O_6$ (454.64): C, 68.69; H, 10.20. Found: C, 68.55; H, 10.05%.

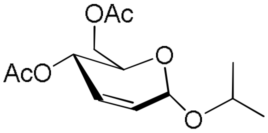
Heptyl 4,6-di-O-acetyl-2,3-dideoxy-α-ᴅ-erythro-hex-2-enopyranoside (**17j**)



(17j)

$[\alpha]_D^{25}$ +68° (*c* 0.15, CH_2Cl_2); **IR** (KBr): 2928, 2857, 1745, 1369, 1234, 1105, 1039, 908, 802 cm^{-1}; ^{1}**H NMR** (400 MHz, $CDCl_3$): δ 5.98-5.83 (m, 2H), 5.33 (dd, *J* = 11.2 Hz, *J* = 1.2 Hz, 1H), 5.04 (s, 1H), 4.35-4.29 (m, 1H), 4.25 (dd, *J* = 12 Hz, *J* = 2.4 Hz, 1H), 3.87-3.81 (m, 1H), 3.61-3.48 (m, 2H), 2.18 (s, 3H), 2.16 (s, 3H), 1.70-1.63 (m, 3H), 1.38-1.36 (m, 7H), 0.95 (t, 3H); ^{13}**C NMR** (100 MHz, $CDCl_3$): δ 170.9, 170.4, 129.1, 128.2, 94.5, 69.1, 67.0, 65.5, 63.2, 31.9, 29.8, 29.2, 26.3, 22.7, 21.1, 20.9, 14.2. **Anal. Calcd**. for $C_{17}H_{28}O_6$ (328.40): C, 62.17; H, 8.59. Found: C, 62.02; H, 8.44%.

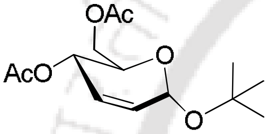
Isopropyl 4,6-di-O-acetyl-2,3-dideoxy-α-ᴅ-erythro-hex-2-enopyranoside (**17k**)



(**17k**)

$[\alpha]_D^{25}$ +112° (*c* 0.18, CH_2Cl_2); **IR** (KBr): 2972, 2931, 1745, 1453, 1371, 1236, 1184, 1125, 1100, 1036, 982, 909, 731, 606 cm^{-1}; ^{1}**H NMR** (400 MHz, $CDCl_3$): δ 5.82-5.73 (m, 2H), 5.23 (d, *J* = 10 Hz, 1H), 5.07 (s, 1H), 4.18 (dd, *J* = 12 Hz, *J* = 6 Hz, 2H), 4.14-4.07 (m, 1H), 3.96-3.90 (m, 1H), 2.03 (s, 3H), 2.02 (s, 3H), 1.20 (d, *J* = 6 Hz, 3H), 1.12 (d, *J* = 6 Hz, 3H); ^{13}**C NMR** (100 MHz, $CDCl_3$): δ 170.8, 170.3, 128.8, 128.5, 92.9, 70.8, 66.8, 65.5, 63.2, 23.6, 22.0, 21.0, 20.8. **Anal. Calcd**. for $C_{13}H_{20}O_6$ (272.29): C, 57.34; H, 7.40. Found: C, 57.20; H, 7.25%.

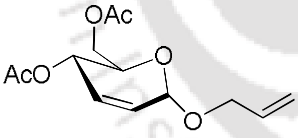
tert-Butyl 4,6-di-O-acetyl-2,3-dideoxy-α-ᴅ-erythro-hex-2-enopyranoside (**17l**)



(**17l**)

$[\alpha]_D^{25}$ +102° (*c* 0.14, CH_2Cl_2); **IR** (KBr): 2976, 2933, 1746, 1437, 1369, 1235, 1195, 1099, 1044, 982, 891, 774, 716, 605 cm^{-1}; ^{1}**H NMR** (400 MHz, $CDCl_3$): δ 5.84 (d, *J* = 10 Hz, 1H), 5.77-5.73 (m, 1H), 5.32 (s, 1H), 5.27 (d, *J* = 8.8 Hz, 1H), 4.26-4.21 (m, 1H), 4.19-4.13 (m, 2H), 2.08 (s, 3H), 2.07 (s, 3H), 1.29 (s, 9H); ^{13}**C NMR** (100 MHz, $CDCl_3$): δ 171.0, 170.6, 129.7, 128.3, 89.1, 75.5, 66.7, 65.5, 63.4, 28.9, 21.1, 21.0. **Anal. Calcd**. for $C_{14}H_{22}O_6$ (286.32): C, 58.73; H, 7.74. Found: C, 58.55; H, 7.57%.

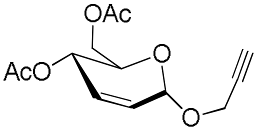
Allyl 4,6-di-O-acetyl-2,3-dideoxy-α-ᴅ-erythro-hex-2-enopyranoside (**17m**)



(**17m**)

$[\alpha]_D^{25}$ +102° (*c* 0.12, CH_2Cl_2); **IR** (KBr): 3081, 2924, 1742, 1652, 1370, 1229, 1101, 1039, 812, 743, 603 cm^{-1}; ^{1}**H NMR** (400 MHz, $CDCl_3$): δ 5.94-5.81 (m, 3H), 5.30-5.24 (m, 2H), 5.18-5.15 (m, 1H), 5.04 (s, 1H), 4.24-4.19 (m, 2H), 4.14 (dd, *J* = 12.4 Hz, *J* = 2.4 Hz, 1H), 4.10-4.02 (m, 2H), 2.06 (s, 3H), 2.04 (s, 3H); ^{13}**C NMR** (100 MHz, $CDCl_3$): δ 170.9, 170.4, 134.2, 129.3, 127.9, 117.6, 93.7, 69.4, 67.0, 65.4, 63.0, 21.0, 20.9. **Anal. Calcd**. for $C_{13}H_{18}O_6$ (270.28): C, 57.77; H, 6.71. Found: C, 57.59; H, 6.78%.

Propynyl 4,6-di-O-acetyl-2,3-dideoxy-α-ᴅ-erythro-hex-2-enopyranoside (**17n**)



(**17n**)

$[\alpha]_D^{25}$ +161° (*c* 0.18, CH_2Cl_2); **IR** (KBr): 3465, 3278, 2917, 1742, 1373, 1229, 1141, 1099, 1039, 965, 909, 731, 680, 613 cm^{-1}; ^{1}**H NMR** (400 MHz, $CDCl_3$): δ 5.92 (d, *J* = 10.4 Hz, 1H), 5.86-5.83 (m, 1H), 5.33 (dd, *J* = 9.6 Hz, *J* = 1.2 Hz, 1H), 5.24 (s, 1H), 4.31

(d, J = 2.4 Hz, 2H), 4.23 (d, J = 4.8 Hz, 1H), 4.18 (dd, J = 12.4 Hz, J = 2.4 Hz, 1H), 4.10-4.07 (m, 1H), 2.52 (t, 1H), 2.10 (s, 3H), 2.09 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 170.6, 170.1, 129.7, 127.2, 92.6, 79.0, 74.9, 67.1, 65.0, 62.7, 54.9, 20.8, 20.7. **Anal. Calcd**. for $C_{13}H_{16}O_6$ (268.26): C, 58.20; H, 6.01. Found: C, 58.01; H, 5.94%.

*XRD for Compounds **17n***

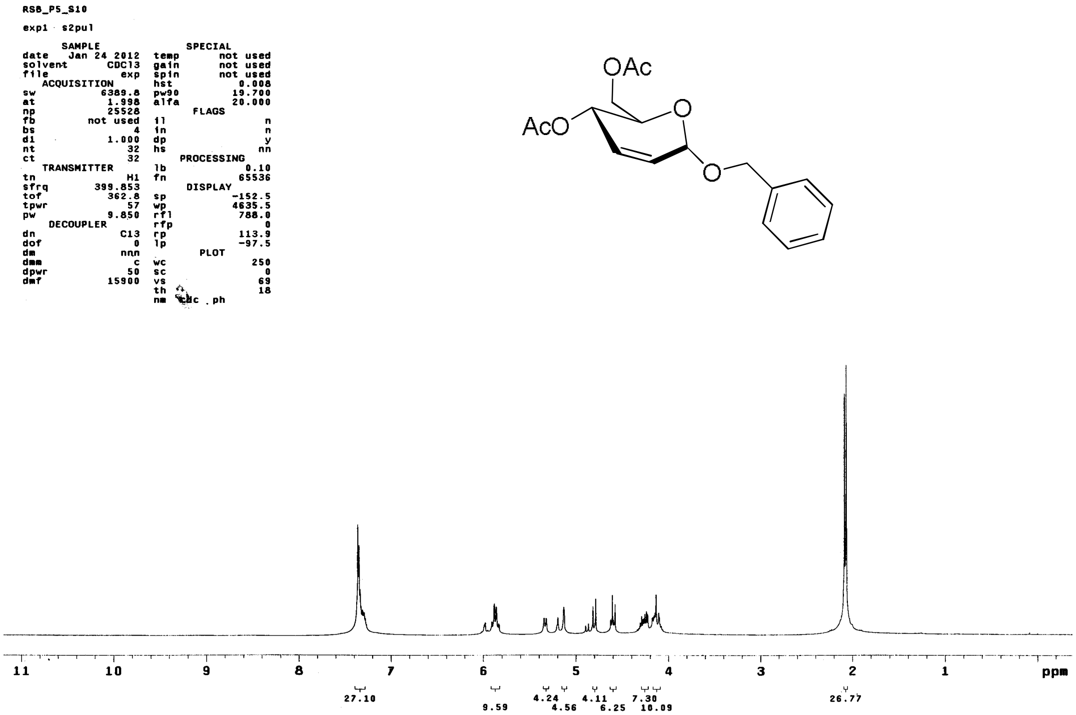
Complete crystallographic data of **17n** for the structural analyses have been deposited with the Cambridge Crystallographic Data Centre, CCDC No. 875412. Copies of this information may be obtained free of charge from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK, (fax: +44-1223-336033, e-mail: deposit@ccdc.cam.ac.uk or via: www.ccdc.cam.ac.uk).

Table 8. Crystal data and structures refinement for the compound **17n**, atomic coordinates, equivalent isotropic displacement parameters and bond angles, please check the CIF.

Parameters	Compound **17n**
Empirical Formula	'$C_{13}H_{16}O_6$'
Formula weight	268.26
Temperature	296 K
CCDC no	875412
Wavelength (Å)	0.71073 Å
Crystal system	Orthorhombic
Space group	P2(1)2(1)2(1)
Radiation type	Mo K\a
Radiation source	'fine-focus sealed tube'
a (Å)	5.2823 (6) Å
b (Å)	15.3302 (18) Å
c (Å)	17.207 (2) Å
α (°)	90.00°
β (°)	90.00°
γ (°)	90.00°
Absolute structure Flack	0.1 (1)
Cell Volume	1393.4 (3) $Å^3$

Z	4
Density	1.279 g/cm^3
μ (mm^{-1})	0.102 mm^{-1}
F(0 0 0)	568.0
Index ranges	-7<=h<=7, -17<=k<=20, -23<=l<=23
Number of unique reflections	3600
Number of parameters	174
Number of restraints	0
Cell Theta range	2.01-21.04°
Measured intensity theta range	1.78- 28.71°
Goodness-of-fit (GOF)[a] on F^2	1.060
Refinement method	Full-matrix least-squares on F2

^{1}H NMR (400 MHz, $CDCl_3$): Benzyl 4,6-di-O-acetyl-2,3-dideoxy-α-ᴅ-erythro-hex-2-eno pyranoside (**17b**)



```
RSB_P5_S10

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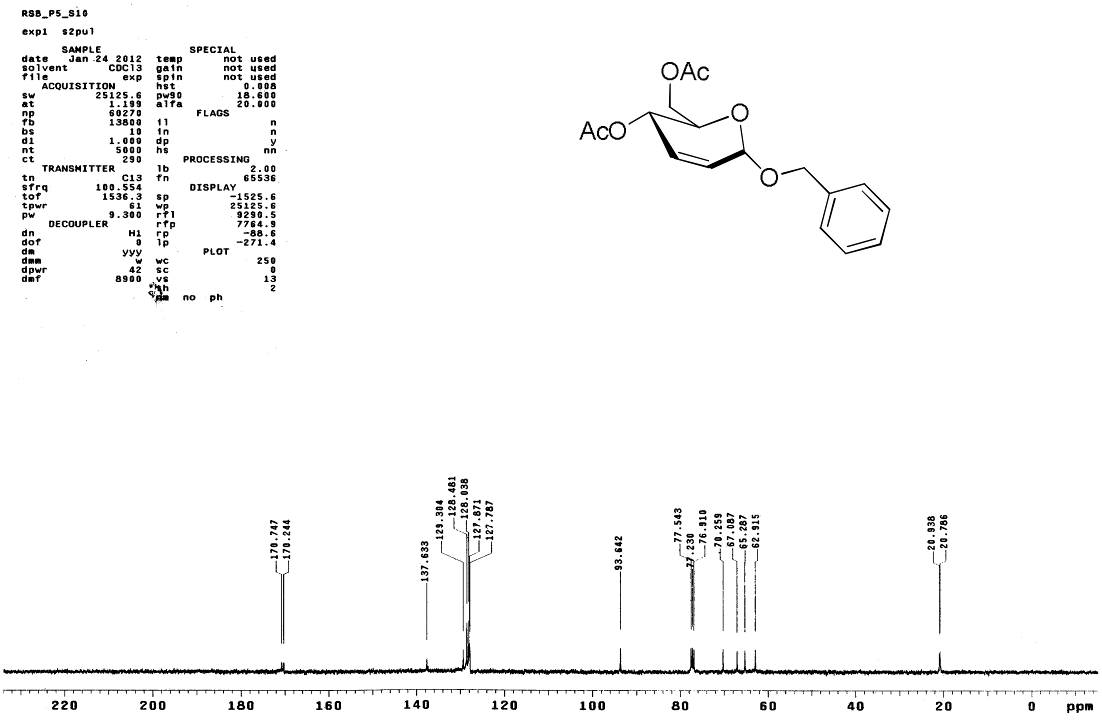
      SAMPLE                 SPECIAL
date   Jan 24 2012   temp        not used
solvent      CDCl3   gain        not used
file           exp   spin        not used
   ACQUISITION       hst            0.008
sw          6389.8   pw90          19.700
at           1.998   alfa          20.000
np           25528         FLAGS
fb        not used   il                 n
bs               4   in                 n
d1           1.000   dp                 y
nt              32   hs                nn
ct              32        PROCESSING
   TRANSMITTER       lb              0.10
tn              H1   fn             65536
sfrq       399.853         DISPLAY
tof          362.8   sp            -152.5
tpwr            57   wp            4635.5
pw           9.850   rfl            788.0
    DECOUPLER        rfp                0
dn             C13   rp             113.9
dof              0   lp             -97.5
dm             nnn           PLOT
dmm              c   wc               250
dpwr            50   sc                 0
dmf          15900   vs                69
                     th                18
                     nm  cdc .ph
```

^{13}C NMR (100 MHz, $CDCl_3$): Benzyl 4,6-di-O-acetyl-2,3-dideoxy-α-ᴅ-erythro-hex-2-eno pyranoside (**17b**)



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RSB_P5_S10

exp1  s2pul

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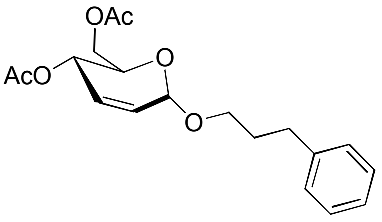
solvent      CDCl3   gain        not used
file           exp   spin        not used
   ACQUISITION       hst            0.008
sw         25125.6   pw90          18.600
at           1.199   alfa          20.000
np           60270         FLAGS
fb           13800   il                 n
bs              10   in                 n
d1           1.000   dp                 y
nt            5000   hs                nn
ct             290        PROCESSING
   TRANSMITTER       lb              2.00
tn             C13   fn             65536
sfrq       100.554         DISPLAY
tof         1536.3   sp           -1525.6
tpwr            61   wp           25125.6
pw           9.300   rfl           9290.5
    DECOUPLER        rfp           7764.9
dn              H1   rp             -88.6
dof              0   lp            -271.4
dm             yyy           PLOT
dmm              w   wc               250
dpwr            42   sc                 0
dmf           8900   vs                13
                     th                 2
                     nm  no  ph
```

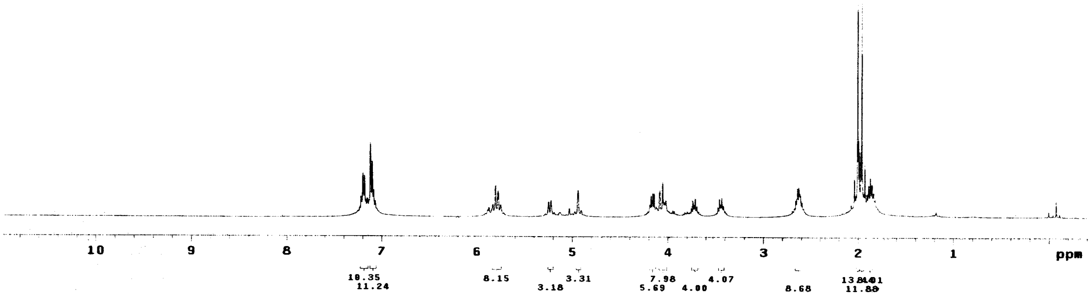
***NMR (400 MHz, CDCl$_3$)**: 3-Phenylpropanyl 4,6-di-O-acetyl-2,3-dideoxy-α-ᴅ-erythro-hex-2-eno pyranoside* (**17d**)

```
RSB_P5_S4

exp1  s2pul

      SAMPLE               SPECIAL
date   Dec 30 2011  temp       not used
solvent      CDCl3  gain       not used
file /export/home/~ spin       not used
ciftemp/RSB_P5_S4_~ hst           0.008
            1H.fid  pw90         19.700
   ACQUISITION      alfa         20.000
sw          6389.8          FLAGS
at           1.998  il                n
np           25528  in                n
fb        not used  dp                y
bs               4  hs               nn
d1           1.000        PROCESSING
nt              32  lb             0.10
ct              32  fn            65536
   TRANSMITTER             DISPLAY
tn              H1  sp           -161.1
sfrq       399.853  wp           4567.6
tof          362.8  rfl           824.3
tpwr            57  rfp               0
pw           9.850  rp            111.0
    DECOUPLER       lp            -96.6
dn             C13           PLOT
dof              0  wc              250
dm             nnn  sc                0
dmm              c  vs               58
dpwr            50  th               35
dmf          15900  nm  cdc  ph
```

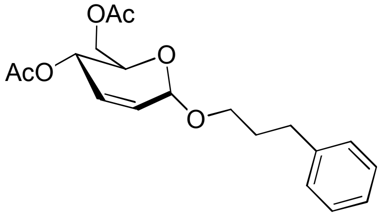


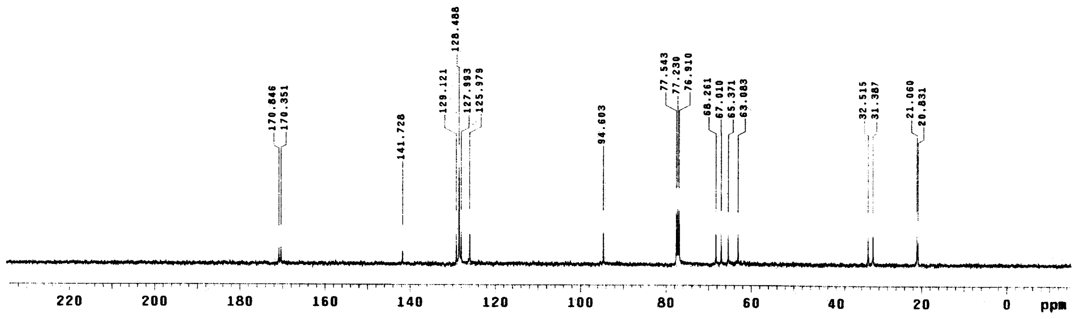


***^{13}C NMR (100 MHz, CDCl$_3$)**: 3-Phenylpropanyl 4,6-di-O-acetyl-2,3-dideoxy-α-ᴅ-erythro-hex-2-enopyranoside* (**17d**)

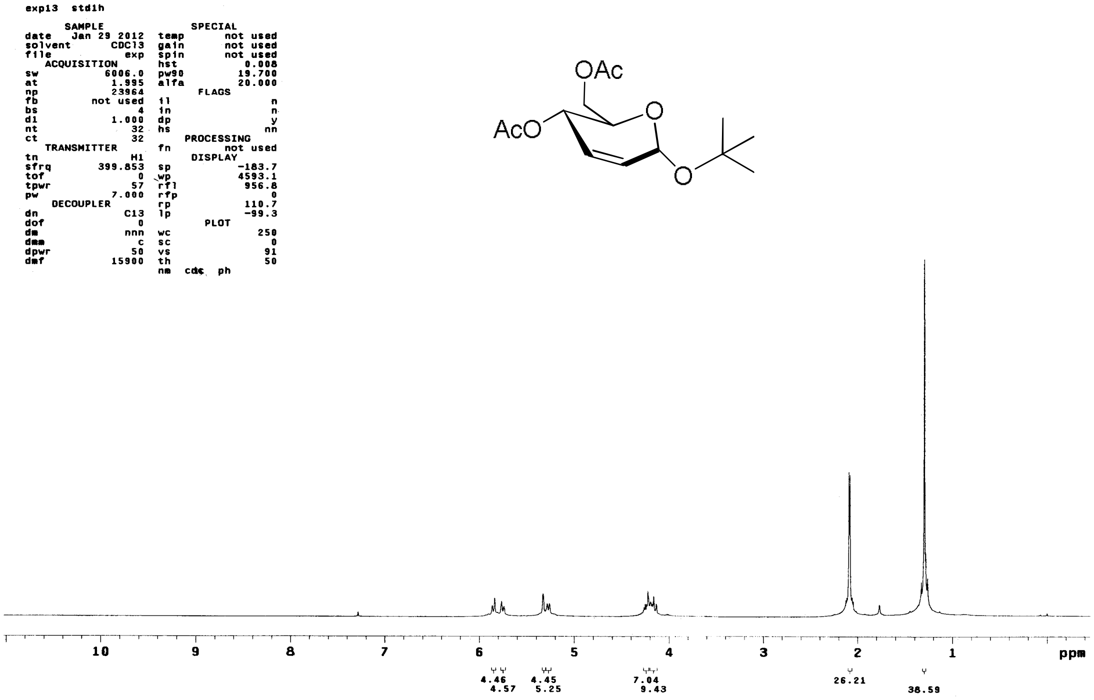
```
exp1  s2pul

      SAMPLE               SPECIAL
date   Dec 29 2011  temp       not used
solvent      CDCl3  gain       not used
file           exp  spin       not used
   ACQUISITION      hst           0.008
sw         25125.6  pw90         18.600
at           1.199  alfa         20.000
np           60270          FLAGS
fb           13800  il                n
bs              10  in                n
d1           1.000  dp                y
nt            5000  hs               nn
ct             840        PROCESSING
   TRANSMITTER      lb             2.00
tn             C13  fn            65536
sfrq       100.554         DISPLAY
tof         1536.3  sp          -1518.7
tpwr            61  wp          25125.6
pw           9.300  rfl          9283.6
    DECOUPLER       rfp          7764.9
dn              H1  rp            -66.0
dof              0  lp           -355.7
dm             yyy           PLOT
dmm              w  wc              250
dpwr            42  sc                0
dmf           8900  vs               22
                    th                3
                    nm  no  ph
```





***^{1}H NMR (400 MHz, CDCl$_3$)**: Tert-Butyl 4,6-di-O-acetyl-2,3-dideoxy-α-ᴅ-erythro-hex-2-eno pyranoside* **(17l)**



```
exp13  stdih

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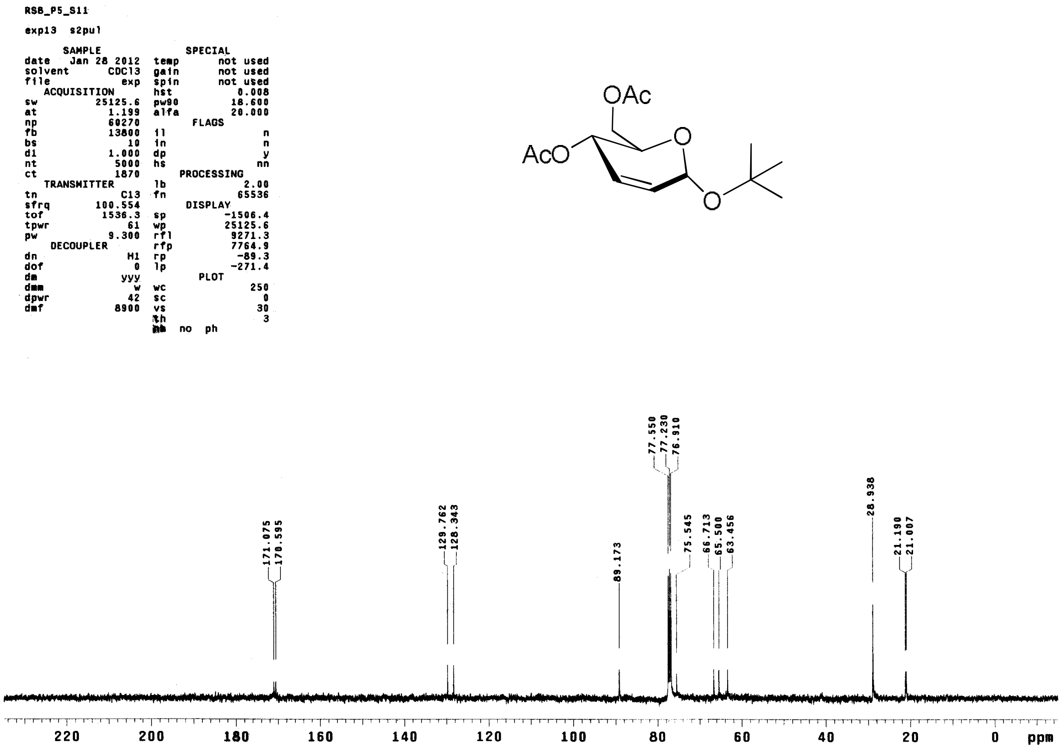
solvent      CDCl3   gain       not used
file           exp   spin       not used
   ACQUISITION       hst           0.008
sw          6006.0   pw90         19.700
at           1.995   alfa         20.000
np           23964          FLAGS
fb        not used   il                n
bs               4   in                n
d1           1.000   dp                y
nt              32   hs               nn
ct              32       PROCESSING
   TRANSMITTER       fn         not used
tn              H1        DISPLAY
sfrq       399.853   sp           -183.7
tof              0   wp           4593.1
tpwr            57   rfl           956.8
pw           7.000   rfp               0
    DECOUPLER        rp            110.7
dn             C13   lp            -99.3
dof              0           PLOT
dm             nnn   wc              250
dmm              c   sc                0
dpwr            50   vs               91
dmf          15900   th               50
                     nm  cdc  ph
```

***^{13}C NMR (100 MHz, CDCl$_3$)**: Tert-Butyl 4,6-di-O-acetyl-2,3-dideoxy-α-ᴅ-erythro-hex-2-eno pyranoside* **(17l)**



```
RSB_P5_S11

exp13  s2pul

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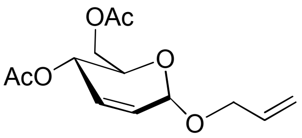
solvent      CDCl3   gain       not used
file           exp   spin       not used
   ACQUISITION       hst           0.008
sw         25125.6   pw90         18.600
at           1.199   alfa         20.000
np           60270          FLAGS
fb           13800   il                n
bs              10   in                n
d1           1.000   dp                y
nt            5000   hs               nn
ct            1870       PROCESSING
   TRANSMITTER       lb             2.00
tn             C13   fn            65536
sfrq       100.554        DISPLAY
tof         1536.3   sp          -1506.4
tpwr            61   wp          25125.6
pw           9.300   rfl          9271.3
    DECOUPLER        rfp          7764.9
dn              H1   rp            -89.3
dof              0   lp           -271.4
dm             yyy           PLOT
dmm              w   wc              250
dpwr            42   sc                0
dmf           8900   vs               30
                     th                3
                     nm  no  ph
```

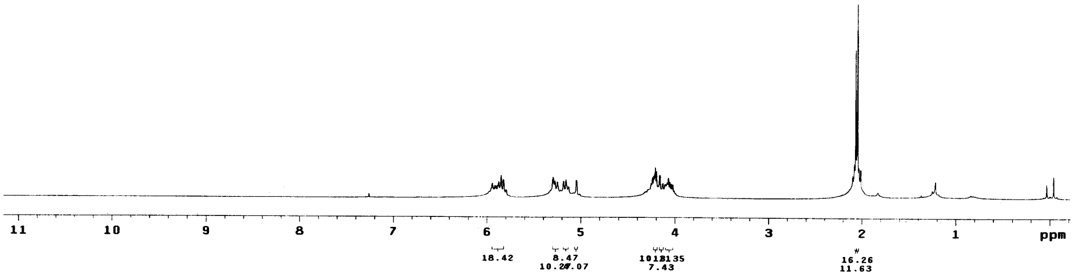
***^{1}H NMR (400 MHz, $CDCl_3$)**: Allyl 4,6-di-O-acetyl-2,3-dideoxy-α-ᴅ-erythro-hex-2-enopyranoside* (**17m**)

```
RSB_P5_S2

expl  s2pul

      SAMPLE                  SPECIAL
date    Dec 21 2011   temp        not used
solvent       CDCl3   gain        not used
file            exp   spin        not used
   ACQUISITION        hst            0.008
sw           6389.8   pw90          19.700
at            1.998   alfa          20.000
np            25528          FLAGS
fb         not used   il                 n
bs                4   in                 n
d1            1.000   dp                 y
nt               32   hs                nn
ct               32        PROCESSING
   TRANSMITTER        lb              0.10
tn               H1   fn             65536
sfrq        399.853          DISPLAY
tof           362.8   sp             -89.7
tpwr             57   wp            4560.4
pw            9.850   rfl            795.8
    DECOUPLER         rfp                0
dn              C13   rp             110.0
dof               0   lp             -64.0
dm              nnn           PLOT
dmm               c   wc               250
dpwr             50   sc                 0
dmf           15900   vs                52
                      th                20
                      nm  cdc  ph
```

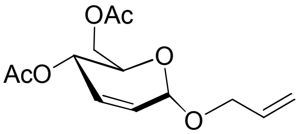


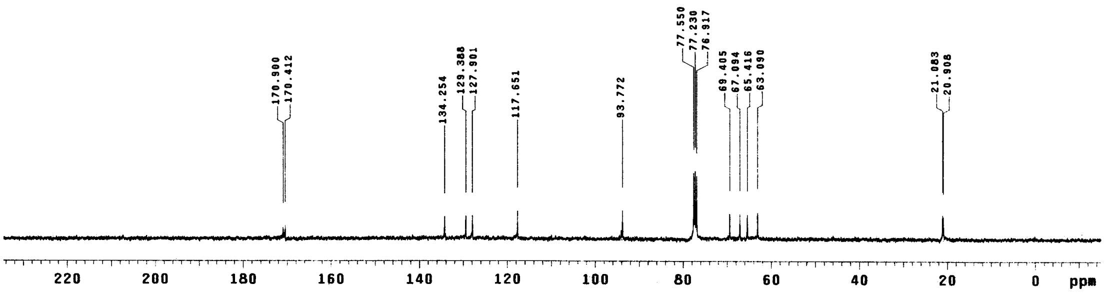


***NMR (100 MHz, $CDCl_3$)**: Allyl 4,6-di-O-acetyl-2,3-dideoxy-α-ᴅ-erythro-hex-2-enopyranoside* (**17m**)

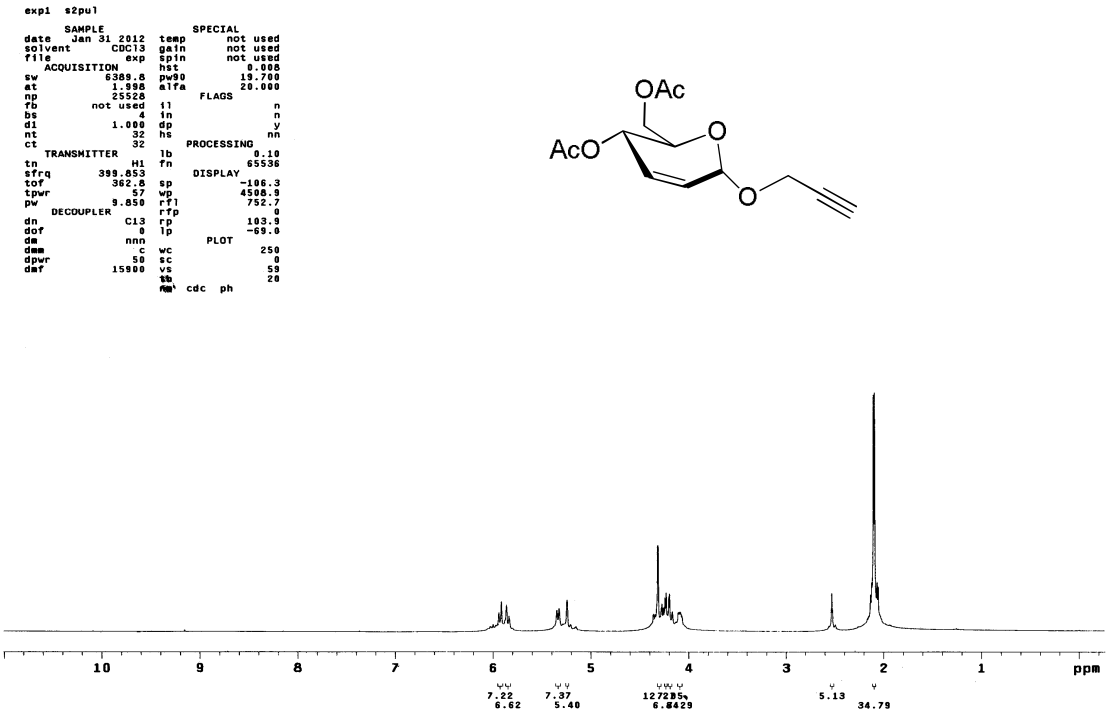
```
expl  s2pul

      SAMPLE                  SPECIAL
date    Dec 21 2011   temp        not used
solvent       CDCl3   gain        not used
file            exp   spin        not used
   ACQUISITION        hst            0.008
sw          25125.6   pw90          18.600
at            1.199   alfa          20.000
np            60270          FLAGS
fb            13800   il                 n
bs               10   in                 n
d1            1.000   dp                 y
nt             5000   hs                nn
ct             1790        PROCESSING
   TRANSMITTER        lb              2.00
tn              C13   fn             65536
sfrq        100.554          DISPLAY
tof          1536.3   sp           -1510.3
tpwr             61   wp           25125.6
pw            9.300   rfl           9275.2
    DECOUPLER         rfp           7764.9
dn               H1   rp             -88.6
dof               0   lp            -271.4
dm              yyy           PLOT
dmm               w   wc               250
dpwr             42   sc                 0
dmf            8900   vs                15
                      th                 2
                      nm  no  ph
```





^{1}H NMR (400 MHz, CDCl$_3$)*: Propynyl 4,6-di-O-acetyl-2,3-dideoxy-α-ᴅ-erythro-hex-2-eno pyranoside* (**17n**)



```
exp1  s2pul

      SAMPLE               SPECIAL
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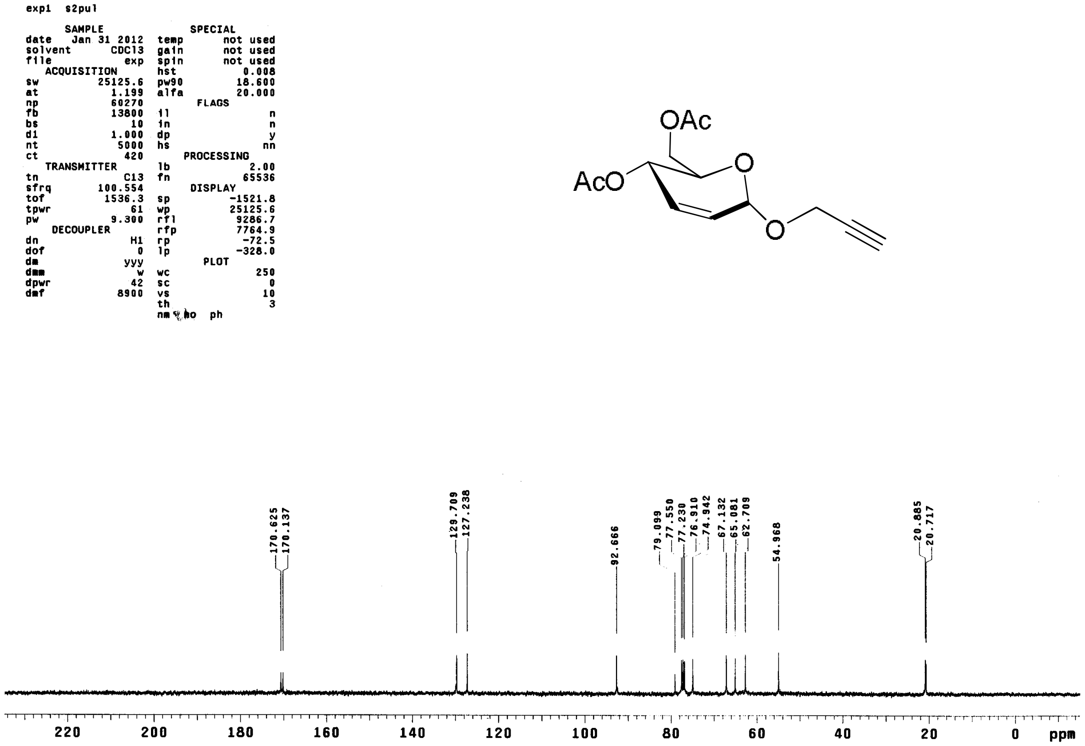
solvent      CDCl3  gain        not used
file           exp  spin        not used
   ACQUISITION      hst            0.008
sw          6389.8  pw90          19.700
at           1.998  alfa          20.000
np           25528          FLAGS
fb        not used  il                 n
bs               4  in                 n
d1           1.000  dp                 y
nt              32  hs                nn
ct              32        PROCESSING
   TRANSMITTER      lb              0.10
tn              H1  fn             65536
sfrq       399.853         DISPLAY
tof          362.8  sp            -106.3
tpwr            57  wp            4508.9
pw           9.850  rfl            752.7
    DECOUPLER       rfp                0
dn             C13  rp             103.9
dof              0  lp             -69.0
dm             nnn           PLOT
dmm              c  wc               250
dpwr            50  sc                 0
dmf          15900  vs                59
                    th                20
                    nm  cdc  ph
```

^{13}C NMR (100 MHz, CDCl$_3$)*: Propynyl 4,6-di-O-acetyl-2,3-dideoxy-α-ᴅ-erythro-hex-2-eno pyranoside* (**17n**)



```
exp1  s2pul

      SAMPLE               SPECIAL
date   Jan 31 2012  temp        not used
solvent      CDCl3  gain        not used
file           exp  spin        not used
   ACQUISITION      hst            0.008
sw         25125.6  pw90          18.600
at           1.199  alfa          20.000
np           60270          FLAGS
fb           13800  il                 n
bs              10  in                 n
d1           1.000  dp                 y
nt            5000  hs                nn
ct             420        PROCESSING
   TRANSMITTER      lb              2.00
tn             C13  fn             65536
sfrq       100.554         DISPLAY
tof         1536.3  sp           -1521.8
tpwr            61  wp           25125.6
pw           9.300  rfl           9286.7
    DECOUPLER       rfp           7764.9
dn              H1  rp             -72.5
dof              0  lp            -328.0
dm             yyy           PLOT
dmm              w  wc               250
dpwr            42  sc                 0
dmf           8900  vs                10
                    th                 3
                    nm  ho  ph
```

Chapter I-III

References

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Brief Literature Survey on Isocyanide-based Multicomponent Reactions

Chapter IV

1.1 Introduction

Novel synthetic methodologies are highly desirable in recent times. Owing to their economic constraints and environmental implications, synthetic chemist are keen to look for an easier and simpler novel procedures.[1] Indeed, MCRs[2] are found to be well-designed synthetic strategies which can accomplish this challenging task in a single operation. By definition "*Multicomponent reactions (MCRs) are convergent reactions, in which three or more starting materials react to form a product, where basically all or most of the atoms contribute to the newly formed product."- Ivar Ugi.*[3] The schematic representation of the defined MCRs is shown in Figure 5.

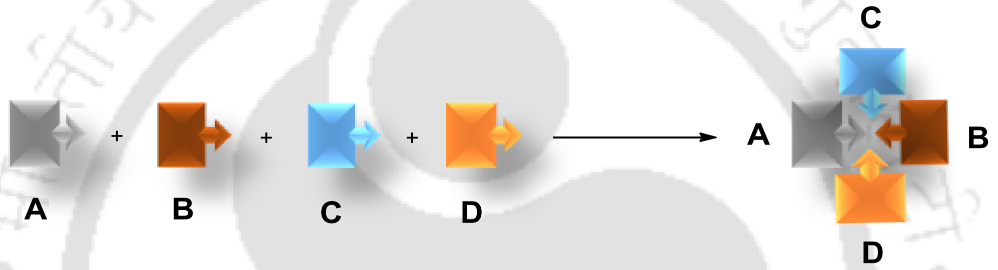


Figure 5. Multicomponent reactions

One-pot MCRs approaches are much easier to execute than a complicated multistep synthesis as depicted in Figure 6. The synthesis of the complex molecule with high stereo-, regio- and chemo selectivity is achieved through multicomponent reactions.[4] MCRs render a facile access to high convergence and efficient synthesis of diverse molecules[5] and this attribute of MCRs make them superior from other synthetic reactions.

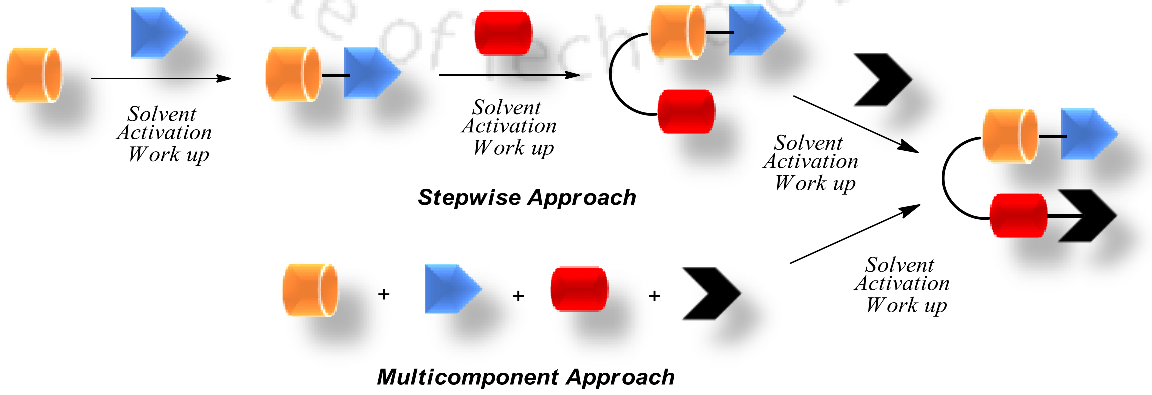


Figure 6. Stepwise *vs* Multicomponent Approach

Multicomponent reaction promote the synthesis of structurally complex architecture molecules in easier synthetic pathway.[6] In addition to that, MCRs are particularly deployed in synthetic pharmaceuticals.[7] Scaffolds assembled from MCRs are found to be potent drugs which are extensively utilized in biomedical applications.[8] The historical overview of MCRs[9-14] is shown in Figure 7.

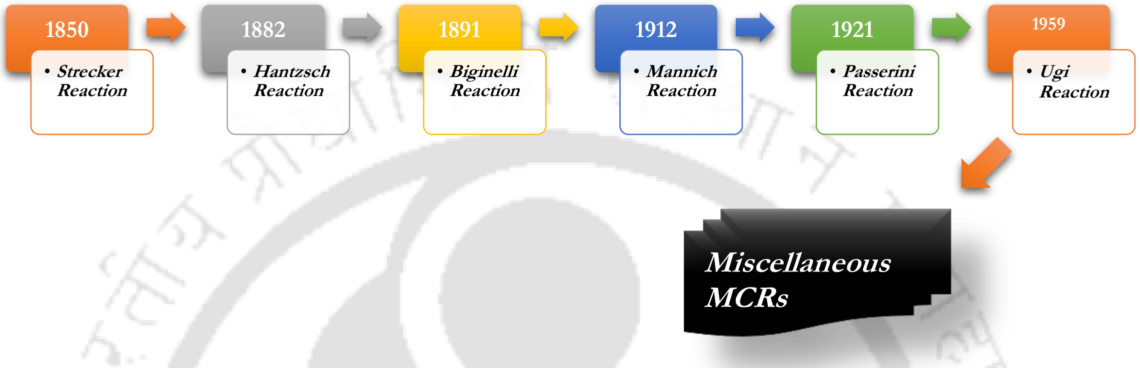
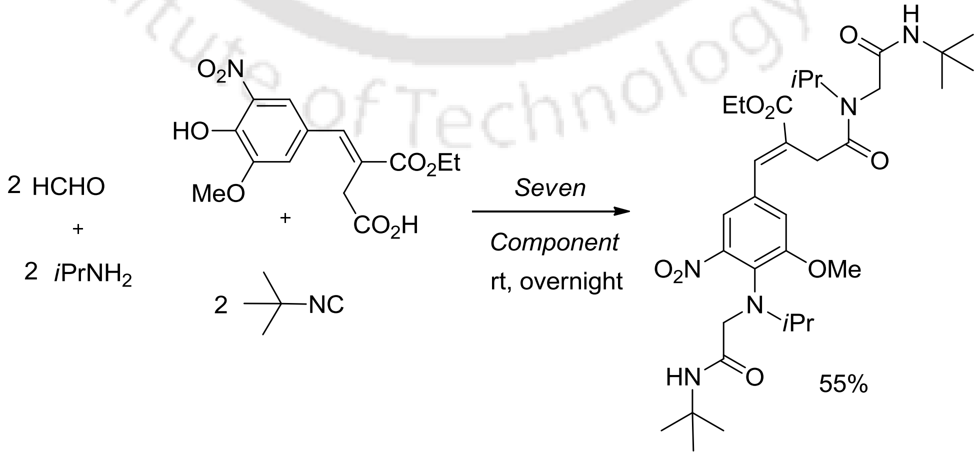


Figure 7. Historical overview of MCRs

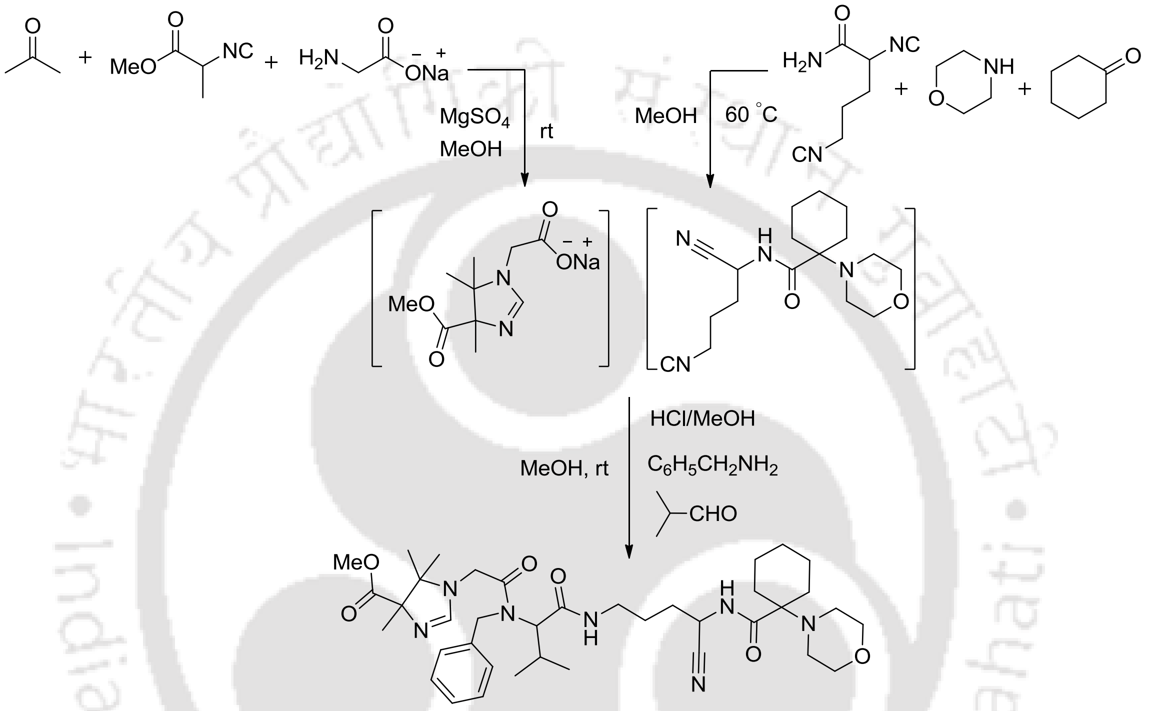
1.2 Recent Development of MCRs

Brauch *et al.*[15] demonstrated that caffeic acid derivative reacts with formaldehyde, isopropyl amine and *tert*-butyl isonitrile in a one-pot sequential seven component reaction to afford Ugi-Mumm/Ugi–Smiles product in 55% yield. Overall eight new covalent bonds were formed in this seven component reaction which is shown in Scheme 42.



Scheme 42

Orru *et al.*[16] developed a one-pot eight component reaction from two three-component followed by one four-component reactions which led to an overall eight component product. The resultant product endures with nine new covalent bonds formation. Eventually, this is the only methodology which reports highest number of component reactions i.e. eight till date in literature as depicted in Scheme 43.



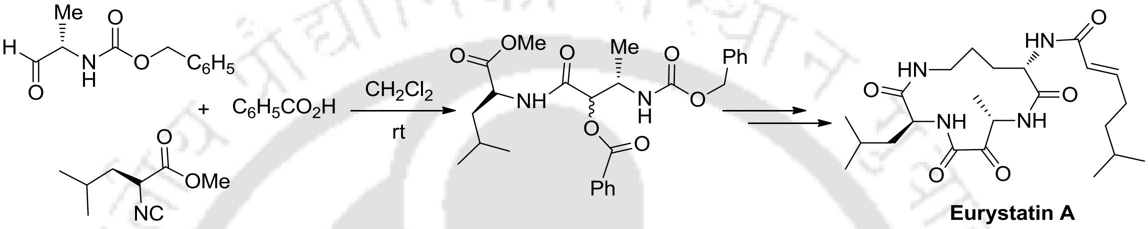
Scheme 43

1.3 Isocyanide Based Multicomponent reactions

Isocyanide are found to be most reactive, highly stereo and regioselective, and possess functional groups tolerance and higher bond forming efficiency. Due to their distinct feature, it is extensively utilized in multicomponent reactions. Moreover, it found to be the subclass of multicomponent reactions as Isocyanide based multicomponent reactions (IMCRs).[17] In general, IMCRs are normally rapid and provide diversity for discovery of new heterocyclic entities. However, the pathways of the reacting isocyanides in MCRs might be as electrophile or nucleophile and in some cases as radical reactions. Nowadays, isocyanide based multicomponent reactions are examined as overall extension of Passerini and Ugi reactions.

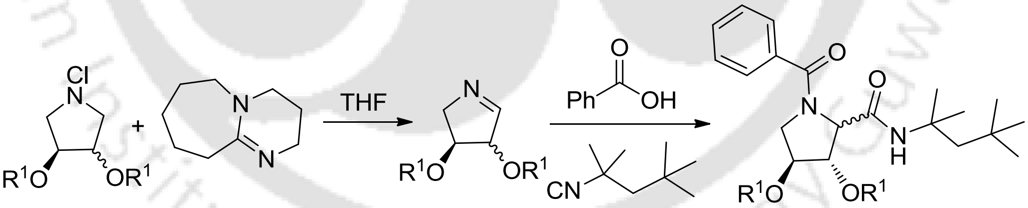
1.3a Synthetic Utility of Three-Component IMCRs

Schmidt and co-workers[18] demonstrated that protected (*S*)-alaninal reacts with (*S*)-2-isocyano-4-methylpentanoate and benzoic acid in dichloromethane at room temperature subject to Passerini product of diastereomeric mixture, which eventually further undergoes three steps to attain a target molecule of eurystatin A as represented in Scheme 44.



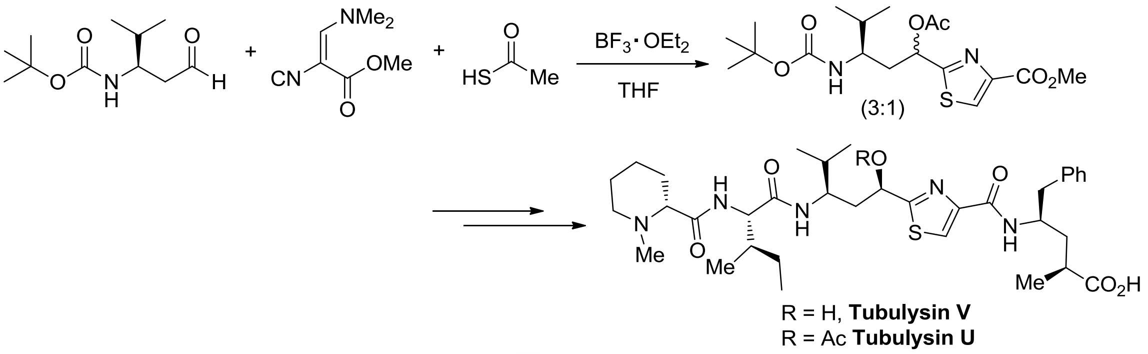
Scheme 44

Davis *et al.*[19] used Joullie´-Ugi reaction to access functionalized azasugar moiety from five membered cyclic imine which is depicted in Scheme 45. Some of the synthesized compounds exhibit a selective antiviral activity.



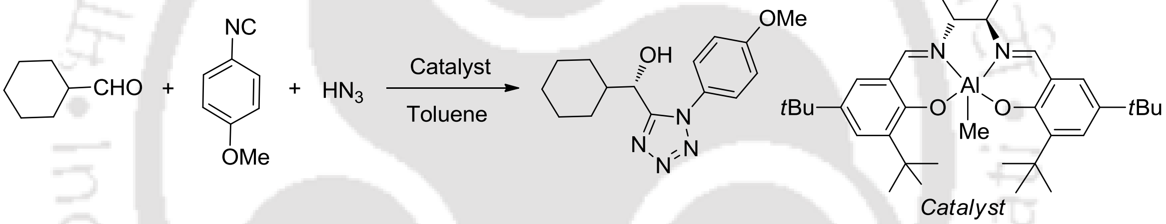
Scheme 45

Domling *et al.*[20] used Passerini-type three-component reaction as a key synthetic intermediate step for the synthesis of tubulysins V and U. Typically, L-*N*-Boc homovaline aldehyde react with thioacetic acid and Schollkopf's isonitrile in presence of boron trifluoride etherate at -78 °C to afford 3:1 diastereomeric mixture of Passerini adduct product which further undergoes several steps to attain target tubulysins V and U as shown in Scheme 46.



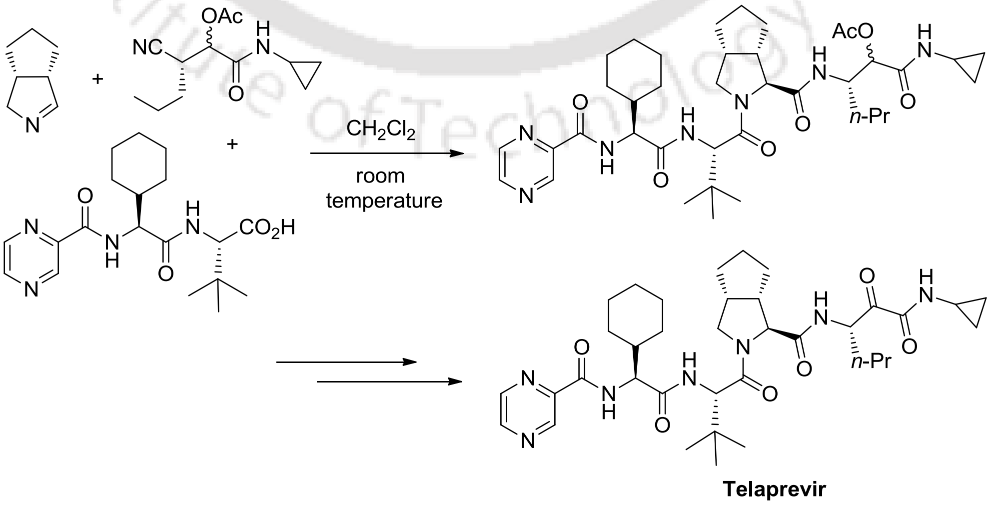
Scheme 46

Zhu *et al.*[21] utilized a three-component Passerini reaction for the construction of enantioselective 5-(1-hydroxyalkyl)tetrazoles from aldehydes, isocyanides, and hydrazoic acid catalyzed by [(salen)Al(III)Me] in toluene with excellent yields as represented in Scheme 47.



Scheme 47

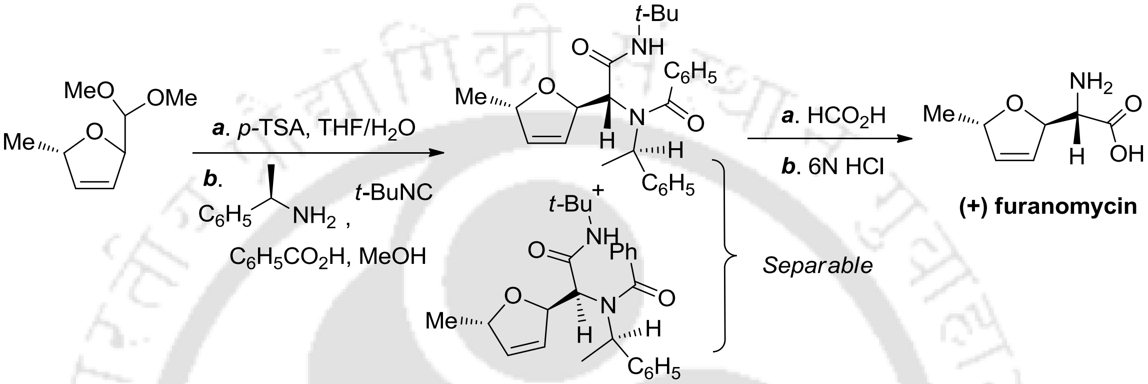
Ruijter *et al.*[22] demonstrated a significant Ugi-type three-component approach used for the synthesis of biologically active synthetic pharmaceutical telaprevir which is shown in Scheme 48.



Scheme 48

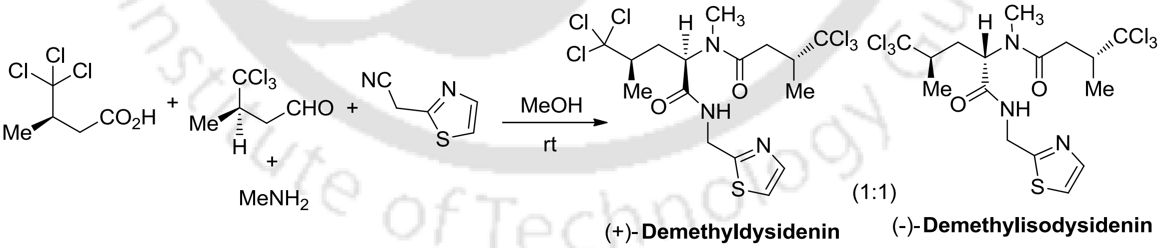
1.3b Synthetic Utility of Four-Component IMCRs

Joullié *et al.*[23] synthesized an antibiotic furanomycin using four component Ugi reaction as a key step. Deprotected furanoacetal react with R-methyl benzylamine, *tert*-butyl isocyanide and benzoic acid led to a mixture of diastereomeric products, which are separable and it further undergoes debenzylation followed by acidic cleavage to furnish the target molecule as shown in Scheme 49.



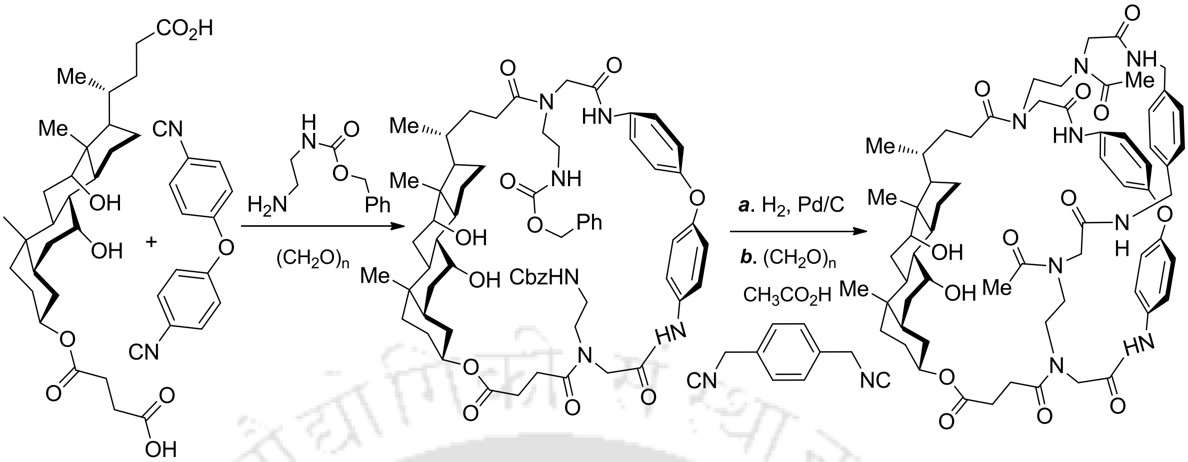
Scheme 49

Williard *et al.*[24] demonstrated the synthesis of (+)-demethyldysidenin and (-)-demethylisodysidenin from synthesized reactants of carboxylic acid and aldehyde with isocyanide and methylamine in methanol at room temperature to access a separable 1:1 diastereomeric products which is shown in Scheme 50.



Scheme 50

Rivera *et al.*[25] established that double Ugi four component reaction were explored for the synthesis of macrobicycle from dicarboxylic acid, formaldehyde, diisocyanide and amine. The first obtained macrocycle containing protected amine were deprotected which led to reactive free amine and subsequently it reacted with different isocyanide for second double Ugi four component reaction which delivered a complex macrobicyclic molecule with 16 new covalent bonds as shown in Scheme 51.



Scheme 51

In general, the above literature survey reveals the growth of the multicomponent reactions in challenging synthetic platform. The theme of the present research work is to synthesize imidazo[1,2-*a*]pyridines and aminoamidine derivatives. The following section discusses their importance along with the synthetic methods:

1.4 Imidazo[1,2-*a*]pyridine Importance

Imidazo[1,2-*a*]pyridine displays a significant role as a pharmacophore and it is extensively utilized in medicinal and synthetic pharmaceuticals.[26-28] A diverse range of molecules possessing imidazo[1,2-*a*]pyridine scaffolds attribute a remarkable attention in biological activities such as antibacterial,[29] antiviral,[30] anti-inflammatory,[31] antihepatitis C,[32] anticonvulsant,[33] antipyretic,[34] antiulcer,[35] antianxiety,[36a] anticancer[36b] hypnotic and cardiotonic agent.[37] It also performs a unique role as calcium channel blockers,[38] cyclin-dependent kinase inhibitors,[39] bradykinin B2 receptor antagonists[40] and amyloid inhibitors.[41] In addition to that, it also act as angiotensin II antagonists,[42] dopamine D4 receptor agonists[43] and 5HT$_3$ antagonists.[44] The most common drugs containing imidazo[1,2-*a*]pyridine skeleton are Zolpidem-treatment of insomnia,[45] Zolimidine-antiulcer agent,[34] Alpidem-anxiolytic agent,[46] and Olprinone-treatment for heart failure[47] which is shown in Figure 8.

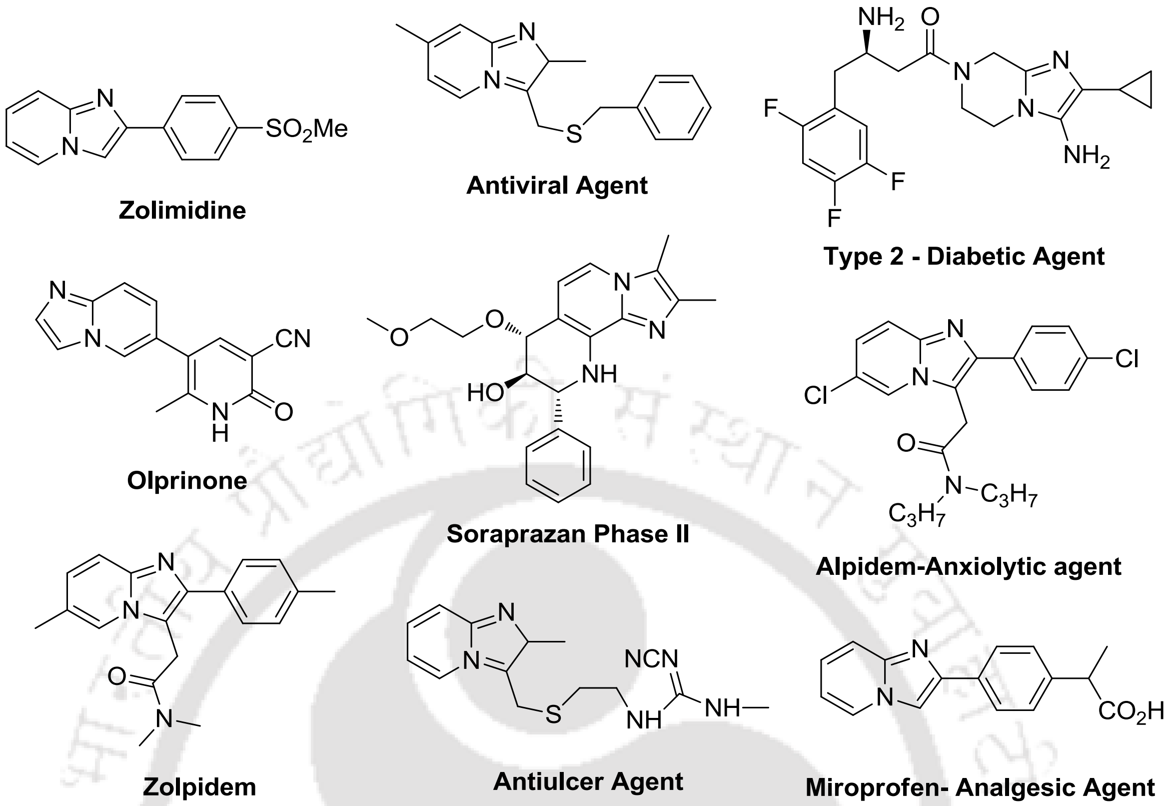
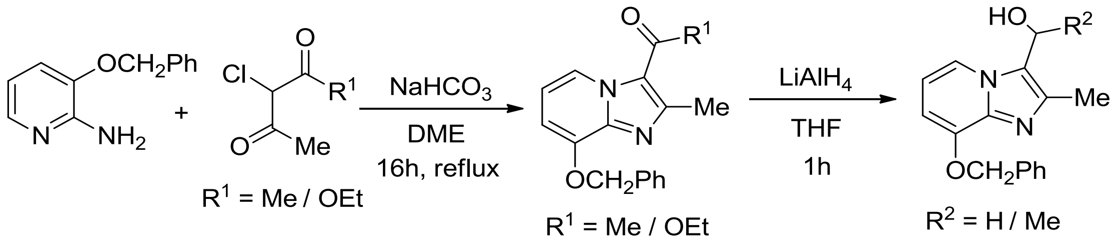


Figure 8. Some of the biologically active compounds containing imidazo[1,2-*a*]pyridine framework

Despite these facts, imidazo[1,2-*a*]pyridine also exhibit an interesting application in material science.[48] Imidazo[1,2-*a*]pyridines are widely used as microglial cell visualization and as probe for benzodiazepine receptors.[49]

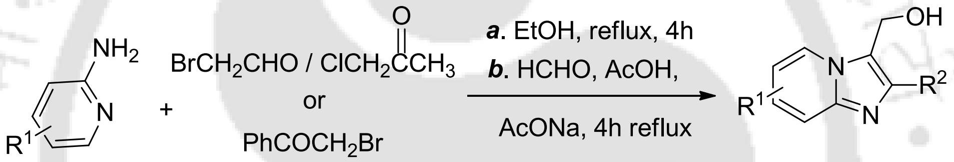
1.4a Synthetic utility of Imidazo[1,2-*α*]pyridines

Starrett *et al.*[50] demonstrated that condensation of 2-aminopyridines with α-chloro-1,3-dicarbonyl compound in DME using sodium bicarbonate under reflux condition led to C-3 carbonyl imidazo[1,2-*a*]pyridine derivatives. The obtained product on reduction with lithium aluminium hydride in tetrahydrofuran which afford hydroxy alkyl imidazo[1,2-*a*]pyridine derivatives is shown in Scheme 52. Further it is elaborate as functionalized primary amine derivative at C-3 position to exhibit as effective antiulcer agents.



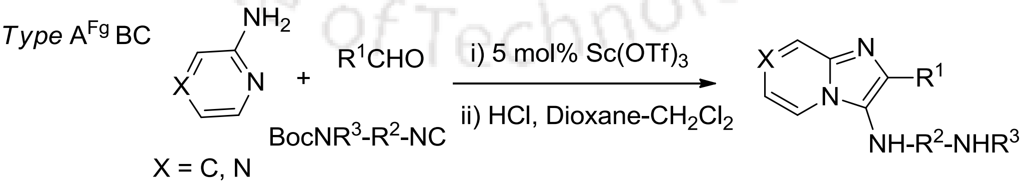
Scheme 52

Gueiffier *et al.*[51] reported that direct hydroxymethylated imidazo[1,2-*a*]pyridines were synthesized using 2-aminopyridines, α-halo-(acetaldehyde/acetone)/phenacyl bromide in ethanol under reflux condition, followed by formaldehyde and sodium acetate in acetic acid which is depicted in Scheme 53. The resulted product tagged with thiol moiety is an important antiviral agent.



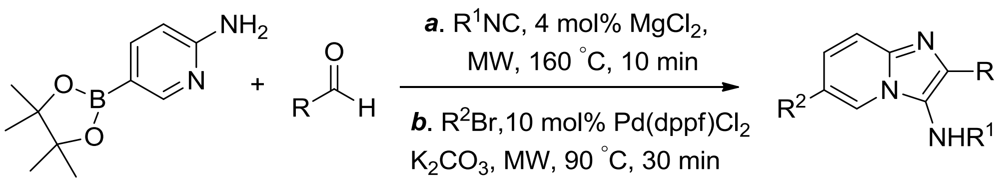
Scheme 53

Bencsik *et al.*[52] developed a diverse range of drug like library $A^{FG}BC$ type imidazo[1,2-*a*]pyridines by employing Boc protected isocyanide, amidine and aldehyde in presence of catalytic amount of scandium triflate. In the subsequent step, cleavage of Boc in acidic medium afforded aminosubstituted imidazo[1,2-*a*]pyridines which is illustrated in Scheme 54.



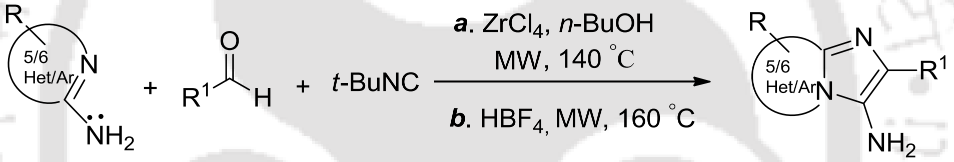
Scheme 54

Dimauro *et al.*[53] explored a microwave-assisted one-pot synthesis of imidazo[1,2-*a*]pyridines via tandem cyclization followed by Suzuki coupling using bifunctionalized 2-aminopyridine-5-boronic ester as key starting material. The significant feature of this reaction is that during cyclization process boronate ester remains unaffected and it is extensively utilized for Suzuki coupling as shown in Scheme 55.



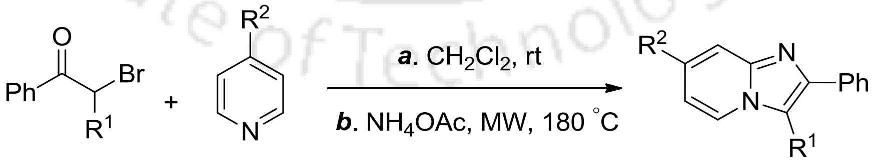
Scheme 55

Guchhait *et al.*[54,36b] demonstrated a microwave assisted Ugi three component reaction for the synthesis of de-*tert*-butylated imidazo[1,2-*a*]pyridines in presence of catalytic amount of Zirconium(IV) chloride along with one equivalent of fluoroboric acid which is shown in Scheme 56.



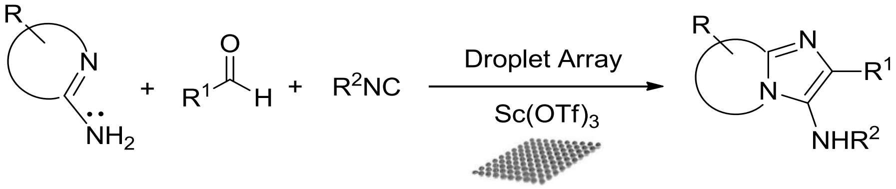
Scheme 56

Adib *et al.*[55] developed a microwave mediated synthesis of imidazo[1,2-*a*]pyridines through in situ generated *N*-phenacylpyridinium bromides, followed by nucleophilic ammonium acetate addition under solvent-free conditions with good yields which is depicted in Scheme 57.



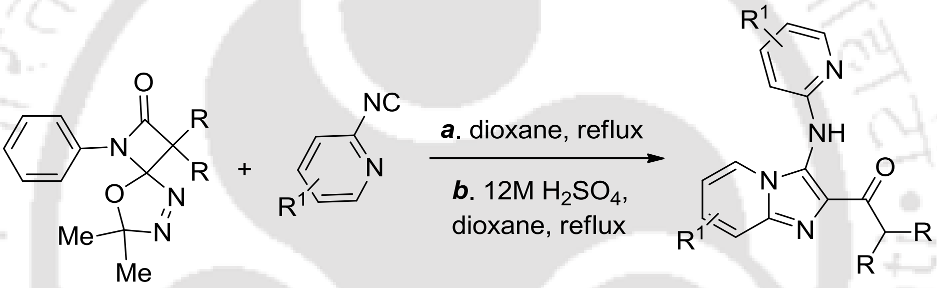
Scheme 57

Balakirev *et al.*[56] developed a drug like fluorophore molecule of imidazo[1,2-*a*]pyridines from Ugi three component reaction of aromatic aldehyde, amidine and isocyanide using droplet array method which is shown in Scheme 58.



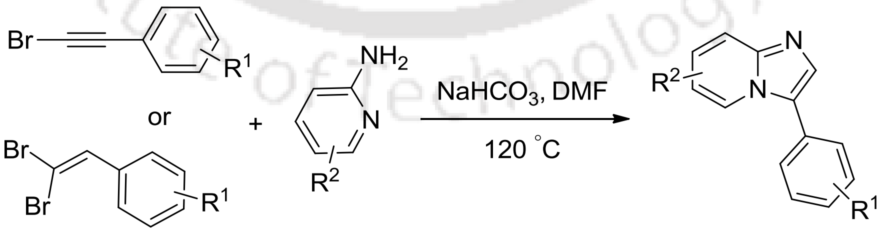
Scheme 58

Cheng *et al.*[57] reported that β-lactam carbenes generated from spiro[β-lactam-4,2’-oxadiazolines] react with 2-pyridyl isonitriles in dioxane under reflux condition, which subsequently undergoes an acid hydrolysis leading to pyridyl based imidazo[1,2-*a*]pyridines as shown in Scheme 59. The resulting product serves as a fluorescence probe for mercury ion.



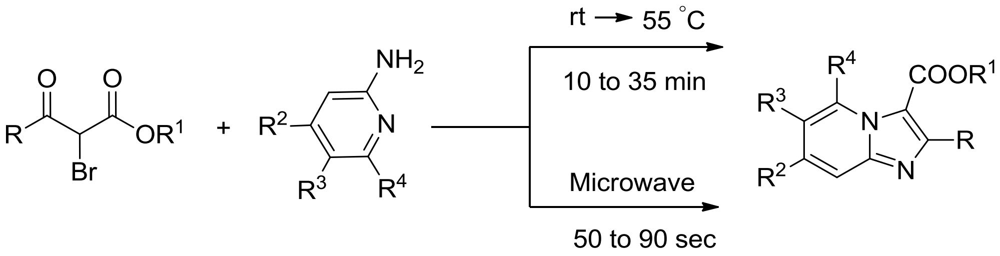
Scheme 59

Zhou *et al.*[58] demonstrated the synthesis of 3-arylimidazo[1,2-*a*]pyridines from 2-aminopyridine, alknyl/alkenyl halide with sodium bicarbonate in DMF at 120 °C with good yields as depicted in Scheme 60.



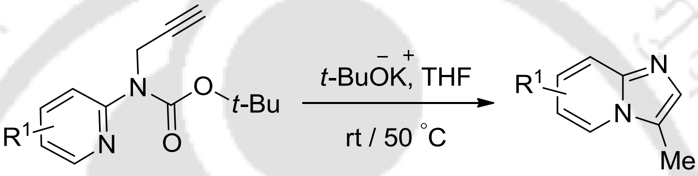
Scheme 60

Adimurthy *et al.*[59] accomplished a solvent-free synthesis of highly substituted imidazo[1,2-*a*]pyridines via thermal and microwave irradiated method using α-bromo-β-keto esters and aminopyridines in shorter reaction time as shown in Scheme 61.



Scheme 61

Savic *et al.*[60] developed an efficient route for the synthesis of imidazo[1,2-*a*]pyridines through base assisted intramolecular cyclization from protected N-propargylated-2-aminopyridine derivatives as represented in Scheme 62.



Scheme 62

Over the years, some other methods were developed for the synthesis of imidazo[1,2-*a*]pyridines using $Sc(OTf)_3$,[61] $ZnCl_2$,[62] Montmorillonite clay K10,[63] ionic liquid,[64] glyoxalic acid[65] and *p*-toluenesulfonic acid.[66] Adib *et al.* developed the synthesis of imidazo[1,2-*a*]pyridine in water.[67] However, the above methods suffer from some of the drawbacks such as harsh reaction conditions, need of expensive and excess amount of catalyst, longer reaction time and awkward work-up procedure. Eventually, still there is a scope to upgrade a new methodology which might work better in terms of yield, reaction condition and substrate scope compatibility.

1.5 Amidine & Aminoamidine Importance

Amidines are extensively utilized for the constructions of nitrogen containing hetero cycles owing to well-designed structural units of bioactive scaffolds.[68] Naturally occurring amidines are Birnbaumins A and B, Efrapeptins, Neoefrapeptins and Pyrostatins A and B which are isolated from microorganisms and Fungi.[69] Flustramine C and Perophoramidine are isolated from Marine Invertebrates.[70] Glomerulatines A-C isolated from higher plants[71] are widely used natural products as well as pharmaceuticals. Hordatine B, Batzelladine B and Agmatine also possess attractive bioactive applications which are all depicted in Figure 9. The important building blocks of the subclass of amidines are α-amino amidines, widely used for the synthesis of antibiotic, antitumor, iminopeptides,[72] Bleomycin,[73] bioluminescence of *Cypridina hilgendorfii* [74]and novacaine derivatives.[75]

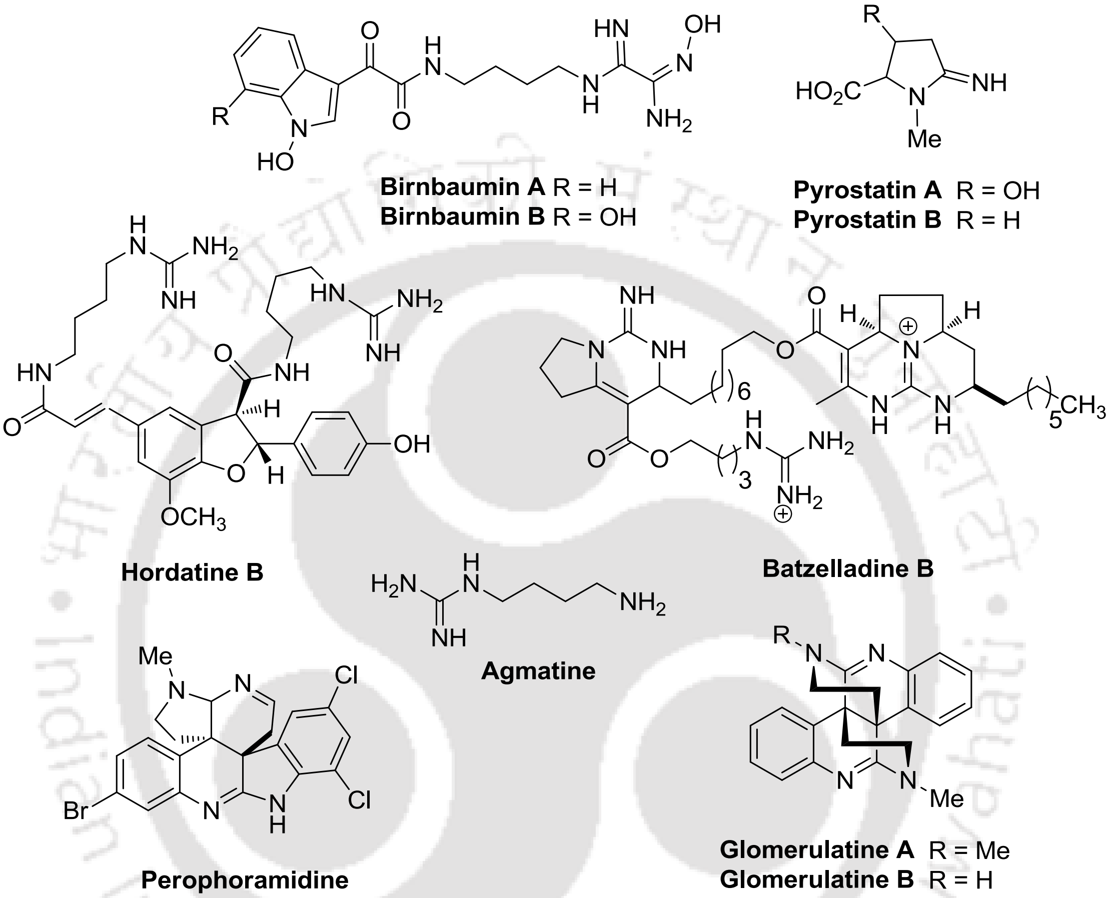
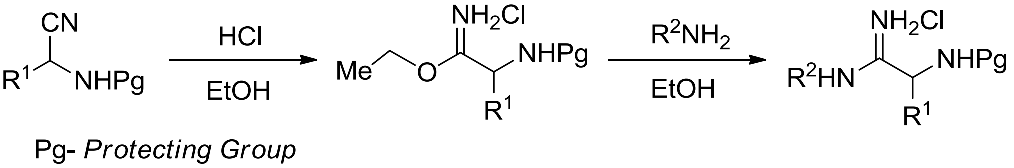


Figure 9. Biologically active compounds containing amidine skeleton

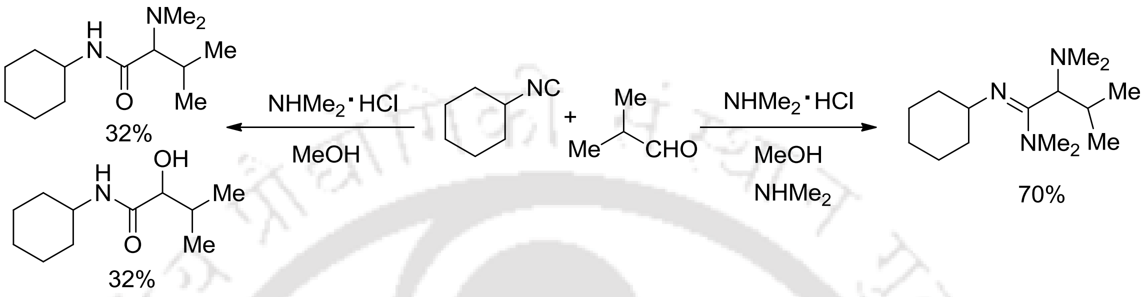
1.5a Amino Amidines Synthetic Methods

Mengelberg *et al.*[76] demonstrated the synthesis of α-amino amidine from N-protected α-amino iminoethers as intermediate followed by amination in ethanol as shown in Scheme 63.



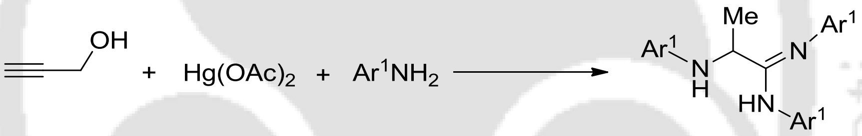
Scheme 63

McFarland *et al.*[77] developed the synthesis of α-amino amidine using cyclohexyl isocyanide, isobutyraldehyde and dimethyl amine in presence of dimethylamine hydrochloride as a catalyst in methanol. However, in absence of dimethyl amine it afforded α-(hydroxyl/dimethylamino) amide compounds with 32% yield each as depicted in Scheme 64.



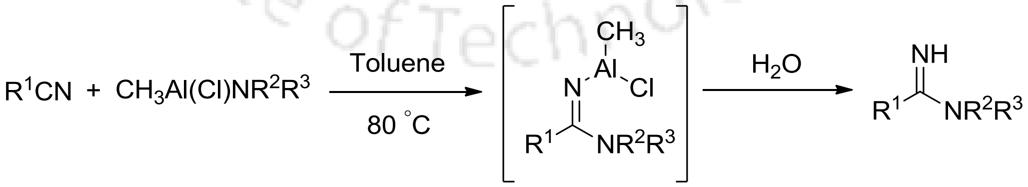
Scheme 64

Barluenga *et al.*[78] accomplished 2-amino-*NN'N''*-triarylpropionamidines using aromatic amines, prop-2-ynol and mercury(II) acetate which is shown in Scheme 65.



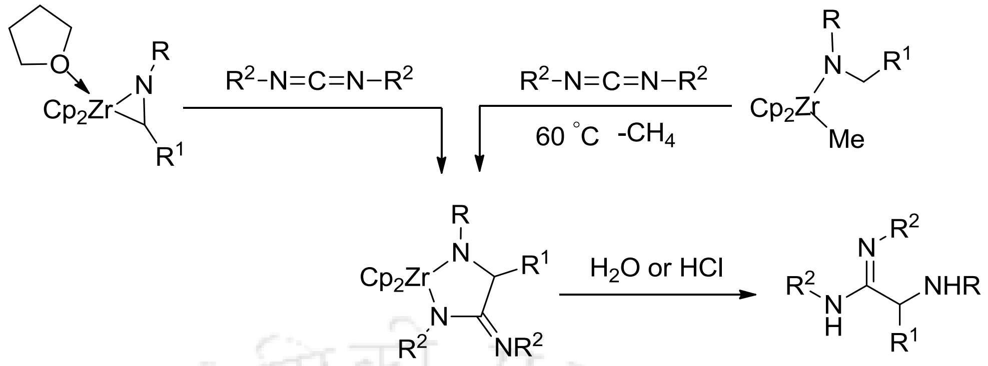
Scheme 65

Garigipati *et al.*[79] established an efficient method for the conversion of nitriles to amidines using alkyl chloroaluminium amide in toluene at 80 °C which is shown in Scheme 66. However, it is also extensively utilized for the synthesis of guanidines from N-substituted cyanamides



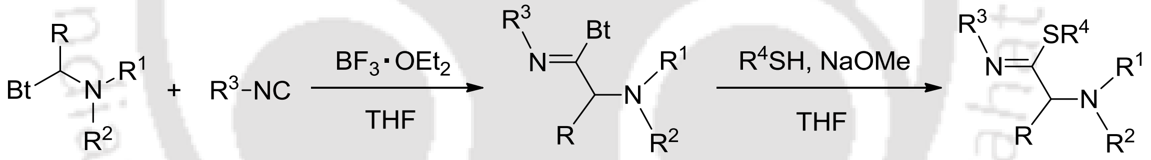
Scheme 66

Norton *et al.*[80] reported that zirconaaziridines reacts with carbodiimides subject to zirconocene-imine complex which eventually undergoes protic cleavage leading to the formation of α-amino amidine. However, zirconaaziridines were also generated *in situ* on thermolysis of $Cp_2Zr[N(R)CH_2(R^1)]Me$ as represented in Scheme 67.



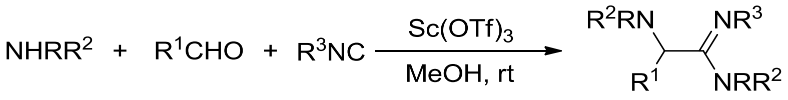
Scheme 67

Katritzky *et al.*[81] described synthesis of highly substituted α-amino-imidoylbenzotriazole using N-(aminoalkyl)benzotriazoles and isocyanide in presence of boron trifluoride as catalyst in THF. The resulting α-amino-imidoylbenzotriazole further undergoes nucleophilic displacement with thiol to form a functionalized α-amino-thioacetimidates as depicted in Scheme 68.



Scheme 68

Recently Keung *et al.*[82] demonstrated a one-pot three-component Ugi condensation reaction for the synthesis of α-amino amidines using secondary amine or primary amine, isobutyraldehyde or aromatic aldehyde and cyclohexyl isocyanide by employing scandium(III) triflate as a catalyst which is shown in Scheme 69.



Scheme 69

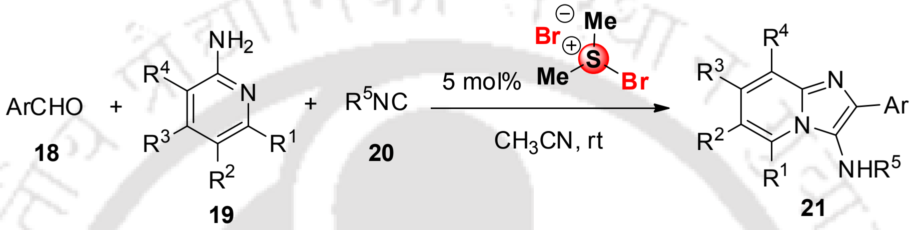
Chapter V

Results and Discussion

Synthesis of Imidazo[1,2-a]pyridines in One-pot three component reaction using Bromodimethylsulfonium bromide (BDMS) as a Catalyst

Results and Discussion

Imidazo[1,2-*a*]pyridine derivatives importance and their synthetic strategies have already been discussed in Chapter IV. In this Chapter an opportune method was devised for the synthesis of imidazo[1,2-*a*]pyridine by employing one-pot three-component reaction by using aromatic aldehyde, aromatic amidine and isocyanide in presence of 5 mol% of bromodimethylsulfonium bromide (BDMS) at room temperature, which is shown in Scheme 70.



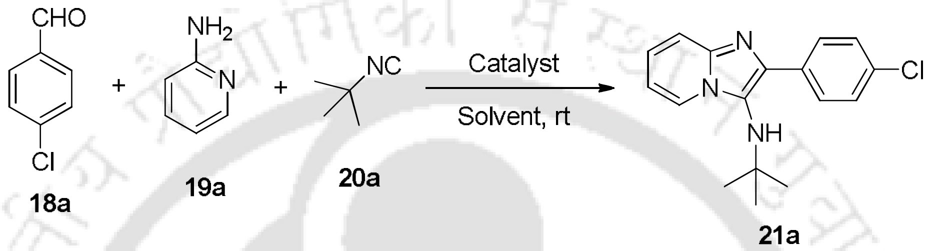
Amidines	**Isocyanides**
19a: R^1= R^2=R^3=R^4=H	**20a**: *tert*-Butyl
19b: R^1=R^3=R^4=H, R^2=Me	**20b**: Cyclohexyl
19c: R^1= R^2=R^3= H, R^4=Me	**20c**: 2-Morpholinoethyl
19d: R^1=R^3=Me, R^2=Br,R^4=H	

Scheme 70. Synthesis of imidazo[1,2-*a*]pyridine derivatives

At the outset, the reaction was performed with *p*-chlorobenzaldehyde (**18a**), amidine (**19a**) and *tert*-butyl isocyanide (**20a**) as a model substrate to find out the optimal reaction condition and the obtained results are summarized in Table 9. Initial screening of Lewis acid catalyst ceric ammonium nitrate (CAN) and Cu(OTf)$_2$ provided lower yield of the product **21a** (Table 9, entry 2 and 3). Moreover, various trial reactions were investigated and we observed that 5 mol% BDMS at room temperature gave the best result in terms of yield and reaction time. However, a systematic evaluation of the various solvent(s) system revealed that acetonitrile was a suitable solvent for the synthesis of imidazo[1,2-*a*]pyridine **21a**.

The optimized protocol was further examined with 4-bromobenzaldeyde, 2-aminopyridine and *tert*-butyl isocyanide in presence of 5 mol% BDMS under similar reaction condition and the corresponding product **21b** were obtained in 85% yield. Similarly, on reaction with 3-hydroxybenzaldehyde, 2-aminopyridine and *tert*-butyl isocyanide gave the required product **21c** with 90% yield. Encouraged by these results, a variety of substituents on the aromatic ring of the aldehyde were treated with 2-amino-5-methylpyridine and *tert*-butyl isocyanide under identical reaction conditions which provided the resulting product **21d-k** in good to excellent yields. It is noteworthy to mention that electron withdrawing substituents on the aldehyde took lesser reaction time as compared to the electron donating group.

Table 9. Optimization of the reaction conditions[a]



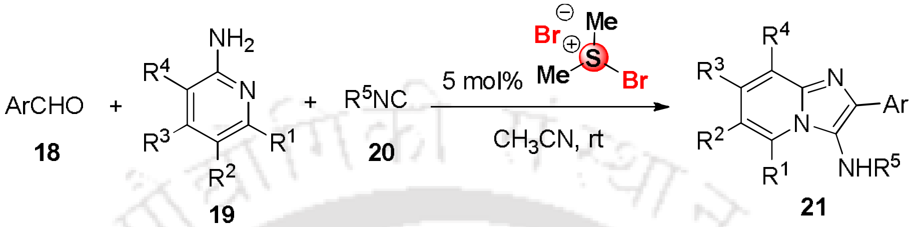
Entry	Catalyst	Solvent	Time (h)	Yield (%)[b]
1	_	CH_3CN	14	26
2	10 mol% CAN	CH_3CN	12	64
3	10 mol% $Cu(OTf)_2$	CH_3CN	9	55
4	5 mol % BDMS	MeOH/DCM	3	75
5	5mol % BDMS	CH_3CN/MeOH	2	85
6	5mol % BDMS	CH_3CN/DCM	2.5	80
7	5mol % BDMS	THF	3.5	77
8	5mol % BDMS	1,4 dioxane	3	72
9	5mol % BDMS	DMF	3.5	68
10	5mol % BDMS	CH_3CN	0.5	95

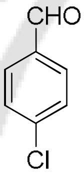
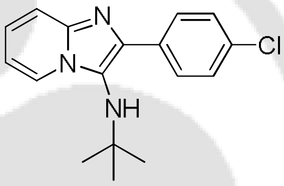
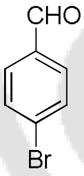
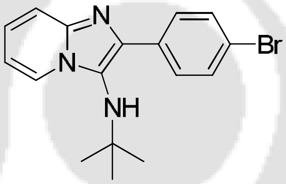
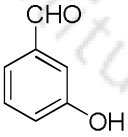
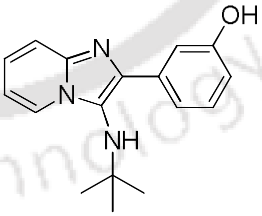
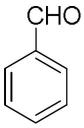
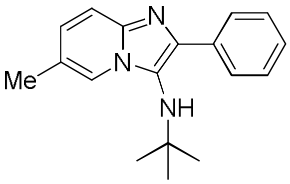
[a]The reaction was performed using 1 mmol scale of *p*-chlorobenzaldehyde, 2-amino pyridine and *tert*-butyl isocyanide at room temperature. [b]Isolated yield.

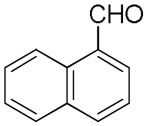
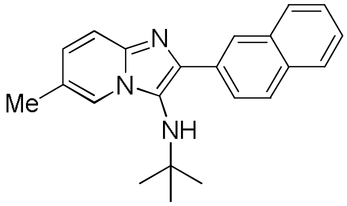
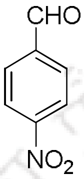
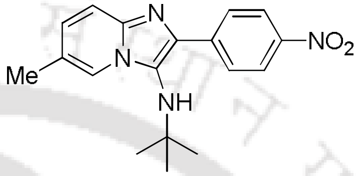
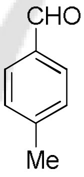
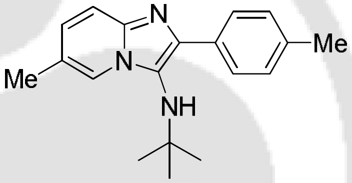
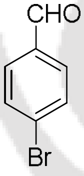
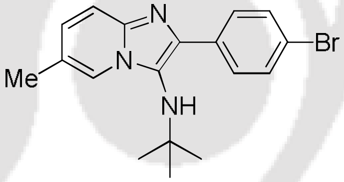
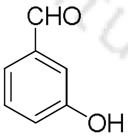
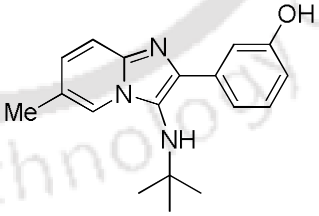
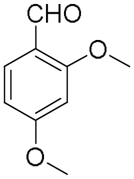
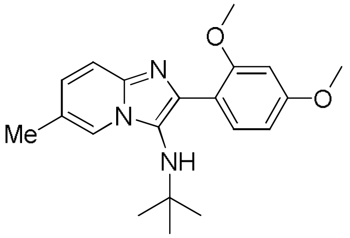
To our delight, next we set to explore the scope of the reaction with 2-amino-3-methylpyridine, 4-chlorobenzaldehyde and cyclohexyl isocyanide with a catalytic amount of BDMS afforded the product **21l** in 90% yield. Subsequently, the steric factor on the substrate was also examined on reaction with sterically hindered 2-amino-5-bromo-4,6-dimethylpyridine, aromatic aldehydes and isocyanides also provided the corresponding product **21m** and **21n** in 87% and 96% yield, respectively. From these successful results, we were motivated to explore the present protocol compatibility with aliphatic aldehyde. Upon reaction with valeraldehyde, 2-amino-5-methylpyridine and 2-

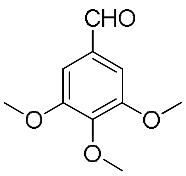
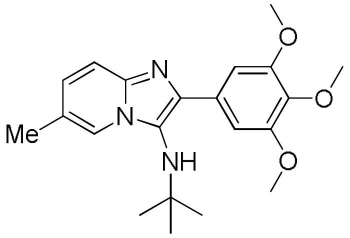
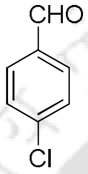
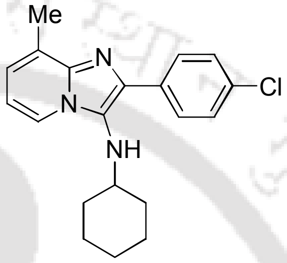
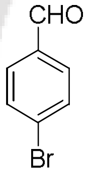
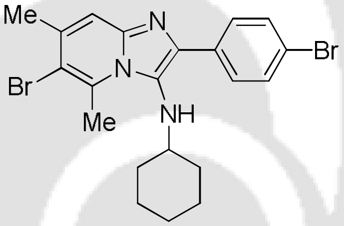
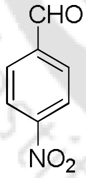
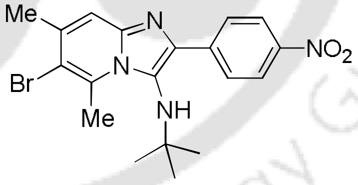
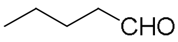
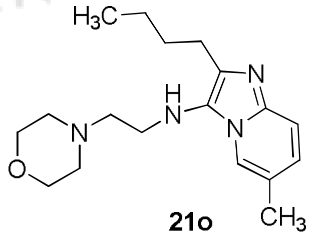
morpholinoethyl isocyanide under similar reaction conditions afforded the resulting product **21o** in good yield. The output of the results indicated that the present protocol work wells with a variety of amidines and aldehydes, which are summarized in Table 10.

Table 10. Synthesis of imidazo[1,2-*a*]pyridines



Entry	Aldehyde (18)	Amidine (19)	R^5NC (20)	Product (21)[a]	Time (h)	Yield (%)[b]
1	 **18a**	**19a**	**20a**	 **21a**	2	95
2	 **18b**	**19a**	**20a**	 **21b**	2	85
3	 **18c**	**19a**	**20a**	 **21c**	2	90
4	 **18d**	**19b**	**20a**	 **21d**	1.5	96

5	 **18e**	**19b**	**20a**	 **21e**	1	93
6	 **18f**	**19b**	**20a**	 **21f**	0.5	94
7	 **18g**	**19b**	**20a**	 **21g**	1	95
8	 **18b**	**19b**	**20a**	 **21h**	2.5	89
9	 **18c**	**19b**	**20a**	 **21i**	1	92
10	 **18h**	**19b**	**20a**	 **21j**	2	85

11	 **18i**	**19b**	**20a**	 **21k**	2.5	88
12	 **18a**	**19c**	**20b**	 **21l**	1.5	90
13	 **18b**	**19d**	**20b**	 **21m**	1.5	87
14	 **18f**	**19d**	**20a**	 **21n**	1	96
15	 **18j**	**19b**	**20c**	 **21o**	2.5	70

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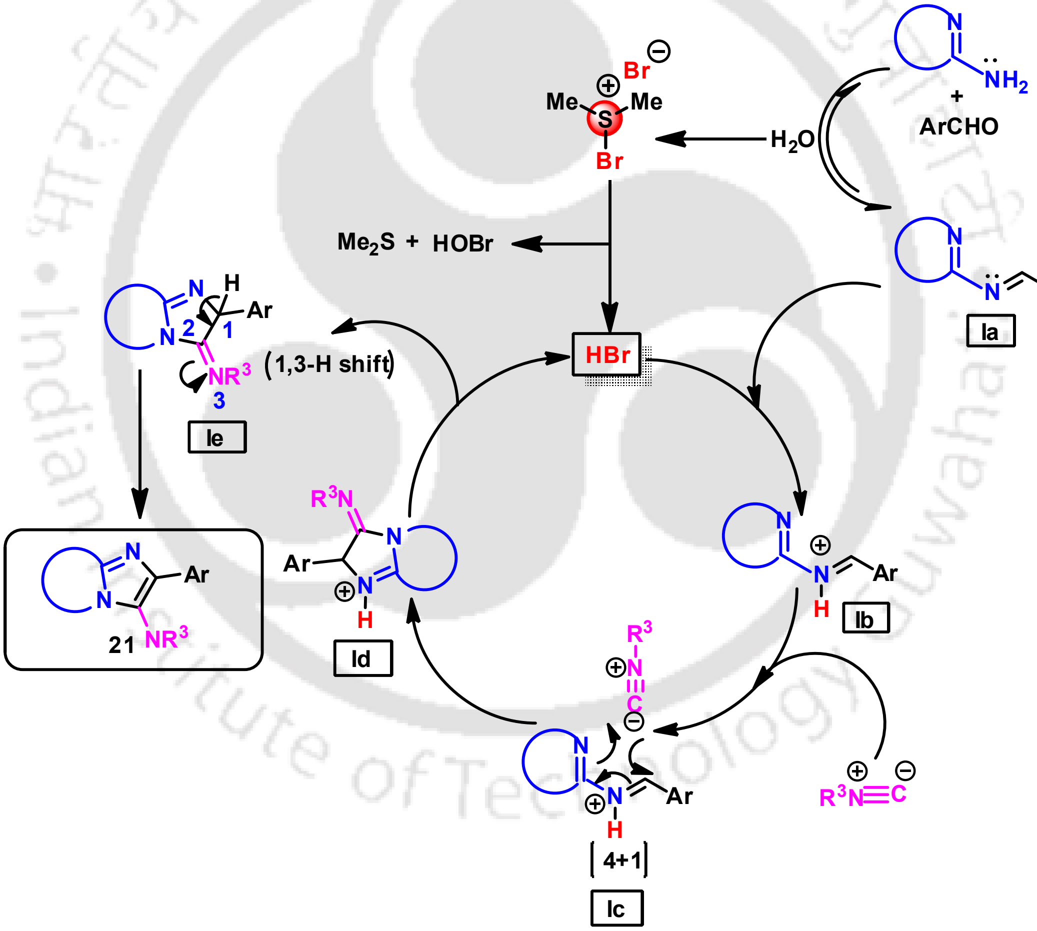
[a]All the reaction was performed using (1mmol) aldehyde, (1mmol) amidine and (1mmol) isocyanide. [b]Isolated yield.

To compare the efficiency of BDMS with aqueous HBr, a reaction was performed with 4-chlorobenzaldeyde, 2-aminopyridine and *tert*-butyl isocyanide using 48% aqueous HBr (0.1 mL) at room temperature and the time taken for the completion of the reaction was 6 h and the product **21a** obtained with lower yield of 65% as compare to BDMS catalyzed reaction. The comparative analysis of the result shows superiority and efficiency of BDMS for the synthesis of imidazo[1,2-*a*]pyridine derivatives.

All the obtained products were characterized by IR, NMR and elemental analyses. Furthermore, the structure of the molecule **21m** was confirmed through single-XRD data which is shown in Figure 10.



Scheme 71. Plausible mechanism for the formation of imidazo[1,2-*a*]pyridines

The mechanism of imidazo[1,2-*a*]pyridine can be described as follows: Amidine reacts with aromatic aldehyde to form imine **Ia** and water. The liberated water molecule reacts with bromodimethylsulfonium bromide (BDMS) to form dimethyl sulfide, HOBr and

HBr. Then, the released HBr undergoes protonation with imine **Ia** to form **Ib**, which further reacts with isocyanide via [4+1] cycloaddition which leads to **Id**. Subsequently, 1,3-hydrogen shift from the intermediate **Ie** gave the final product of imidazo[1,2-*a*]pyridines **21**, as shown in Scheme 71.

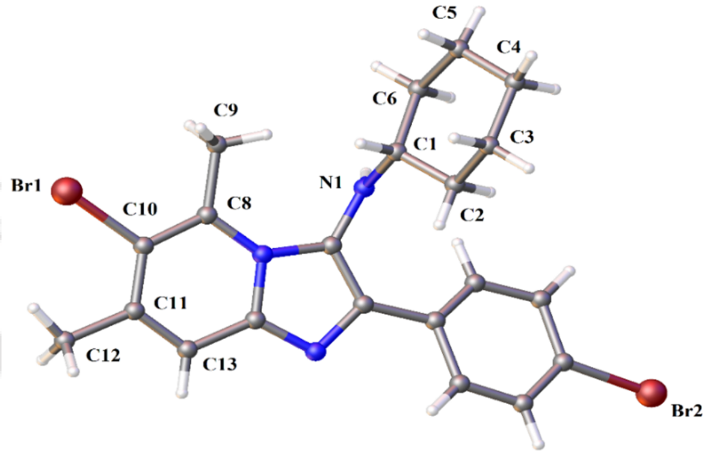


Figure 10. X-ray crystal structure of **21m**

In conclusion, we have explored a mild and facile methodology for the synthesis of imidazo[1,2-*a*]pyridine derivatives by employing aromatic aldehyde, aromatic amidine and isocyanide using BDMS as a catalyst. The merits of the protocol are simple, general, non-aqueous work up, inexpensive, high yield and compatible with wide range of substrates. Furthermore, the synthesized imidazo-heterocyclic scaffold might exist as an interesting pharmacophore in near future.

Experimental Section

Chapter V

Synthesis of Imidazo[1,2-a] pyridines in One-pot three component reaction using Bromodimethylsulfonium bromide (BDMS) as a Catalyst

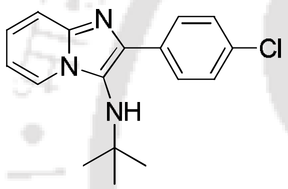
Experimental Section

General procedure for the synthesis of imidazo[1,2-a]pyridine

To a solution of aromatic aldehyde (1 mmol), amidine (1 mmol) and isocyanide (1 mmol) in 2 mL acetonitrile was added 5 mol% bromodimethylsulfonium bromide (0.011 g) at room temperature and allowed to stir for appropriate time as shown in Table 10. After completion of reaction as monitored by TLC, the solid product was filtered off and washed twice with acetonitrile and finally dried under reduced pressure.

Spectral data of Compounds

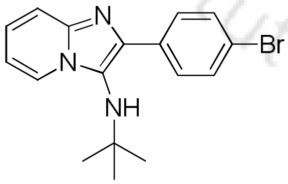
*N-tert-butyl-2-(4-chlorophenyl)H-imidazo[1,2-a]pyridin-3-amine **(21a)***



(21a)

Brown solid, mp 146 °C; **IR** (KBr): 2961, 2925, 2854 cm^{-1}; ^{1}**H NMR** (400 MHz, CDCl$_3$): δ 8.11 (d, J = 6.8 Hz, 1H), 7.87 (d, J = 8.4 Hz, 2H), 7.47 (d, J = 8.8 Hz, 1H), 7.32 (d, J = 8.4 Hz, 2H), 7.07 (t, J = 7.2 Hz, 1H), 6.70 (t, J = 6.8 Hz, 1H), 3.0 (bs, NH, 1H), 0.99 (s, 9H); ^{13}**C NMR** (100 MHz, CDCl$_3$): δ 142.1, 138.4, 133.9, 133.1, 129.4, 128.5, 124.3, 123.6, 123.5, 117.4, 111.5, 56.5, 30.5. **Anal. Calcd** for $C_{17}H_{18}ClN_3$ (299.79): C, 68.11; H, 6.05; N, 14.02. Found: C, 67.95; H, 5.99; N, 13.91.

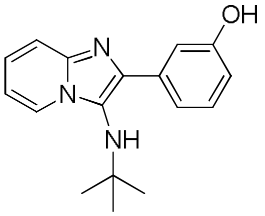
*2-(4-bromophenyl)-N-tert-butylH-imidazo[1,2-a]pyridin-3-amine **(21b)***



(**21b**)

Pale brown solid, mp 146 °C; **IR** (KBr): 3280, 2963, 2923, 1632 cm^{-1}; ^{1}**H NMR** (400 MHz, CDCl$_3$): δ 8.03 (d, J = 6 Hz, 1H), 7.74 (d, J = 8.0 Hz, 2H), 7.39-7.41 (m, 3H), 7.0 (t, J = 8.8 Hz, 1H), 6.61-6.64 (m, 1H), 2.95 (bs, NH, 1H), 0.91 (s, 9H); ^{13}**C NMR** (100 MHz, CDCl$_3$): δ 142.1, 138.3, 134.2, 131.3, 129.7, 124.4, 123.6, 123.4, 121.4, 117.3, 111.5, 56.4, 30.4. **Anal. Calcd** for $C_{17}H_{18}BrN_3$ (344.24): C, 59.31; H, 5.27; N, 12.21. Found: C, 59.05; H, 5.19; N, 12.11.

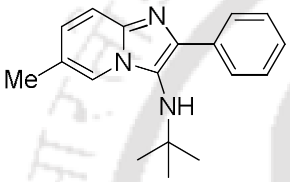
3-(3-(tert-butylamino)H-imidazo[1,2-a]pyridin-2-yl)phenol ***(21c)***



(**21c**)

White solid, mp 126 °C; **IR** (KBr): 3429, 2252, 2130, 1638 cm^{-1}; ^{1}**H NMR** (400 MHz, $CDCl_3$): δ 8.23 (dd, J = 8 Hz, J = 6.8 Hz, 1H), 7.43-7.49 (m, 1H), 7.31-7.36 (m, 2H), 7.09-7.15 (m, 2H), 6.68-6.77 (m, 2H), 4.50 (bs, OH, 1H), 3.60 (bs, NH, 1H), 0.94 (s, 9H); ^{13}**C NMR** (100 MHz, $CDCl_3$): δ 156.1, 140.3, 137.3, 135.0, 128.0, 123.4, 122.9, 122.8, 118.1, 115.4, 114.0, 113.5, 110.3, 55.0, 29.1. **Anal. Calcd** for $C_{17}H_{19}N_3O$ (281.35): C, 72.57; H, 6.81; N, 14.94. Found: C, 72.30; H, 6.73; N, 14.83.

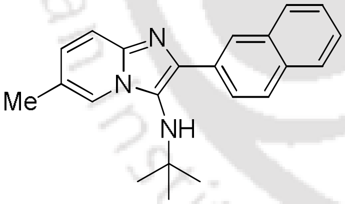
N-tert-butyl-6-methyl-2-phenylH-imidazo[1,2-a]pyridin-3-amine ***(21d)***



(**21d**)

White solid, mp 215-217 °C; **IR** (KBr): 3289, 2968, 2917, 1604 cm^{-1}; ^{1}**H NMR** (400 MHz, $CDCl_3$): δ 7.91 (s, 1H), 7.82 (d, J = 7.6 Hz, 2H), 7.31-7.39 (m, 3H), 7.22 (t, J = 7.2 Hz, 1H), 6.90 (d, J = 9.2 Hz, 1H), 3.0 (bs, NH, 1H), 2.25 (s, 3H), 0.95 (s, 9H); ^{13}**C NMR** (100 MHz, $CDCl_3$): δ 141.3, 139.5, 135.6, 128.3, 128.2, 127.3, 123.4, 121.3, 121.0, 116.8, 56.5, 30.4, 18.5. **Anal. Calcd** for $C_{18}H_{21}N_3$ (279.37): C, 77.38; H, 7.58; N, 15.04. Found: C, 77.13; H, 7.50; N, 14.96.

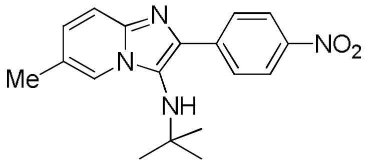
N-tert-butyl-6-methyl-2-(napthalen-2-yl)H-imidazo[1,2-a]pyridin-3-amine ***(21e)***



(**21e**)

White solid, mp 211 °C; **IR** (KBr): 3252, 2972, 2923, 1627 cm^{-1}; ^{1}**H NMR** (400 MHz, $CDCl_3$): δ 8.40 (s, 1H), 8.32 (dd, J = 8.4 Hz, J = 1.6 Hz, 1H), 7.90 (s, 1H), 7.83-7.85 (m, 1H), 7.73-7.79 (m, 2H), 7.38-7.42 (m, 3H), 6.90 (dd, J = 8.8 Hz, J = 1.2 Hz, 1H), 3.23 (bs, NH, 1H), 2.24 (s, 3H), 0.96 (s, 9H); ^{13}**C NMR** (100 MHz, $CDCl_3$): δ 141.1, 138.8, 133.6, 132.8, 132.6, 128.4, 127.7, 127.0, 126.3, 126.1, 125.9, 123.8, 121.2, 116.5, 56.5, 30.5, 18.5. **Anal. Calcd** for $C_{22}H_{23}N_3$ (329.43): C, 80.21; H, 7.04; N, 12.76. Found: C, 79.97; H, 6.97; N, 12.68.

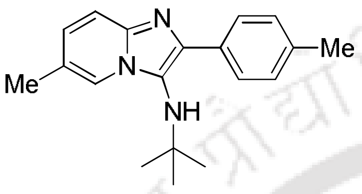
N-tert-butyl-6-methyl-2-(4-nitrophenyl)H-imidazo[1,2-a] pyridin-3-amine ***(21f)***



(**21f**)

Yellow solid, mp 231-232 °C; **IR** (KBr): 3280, 2969, 1629, 1598 cm^{-1}; ^{1}**H NMR** (400 MHz, $CDCl_3$): δ 8.19-8.24 (m, 4H), 7.93 (s, 1H), 7.45 (d, J = 8.8 Hz, 1H), 7.04 (dd, *J* = 8 Hz, *J* = 1.2 Hz, 1H), 3.15 (bs, 1H, NH), 2.34 (s, 3H), 1.06 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$): *δ* 146.7, 141.7, 141.5, 136.5, 128.8, 128.4, 124.8, 123.6, 122.2, 121.2, 117.0, 57.0, 30.6, 18.6. **Anal. Calcd** for $C_{18}H_{20}N_4O_2$ (324.37): C, 66.65; H, 6.21; N, 17.27. Found: C, 66.46; H, 6.13; N, 17.15.

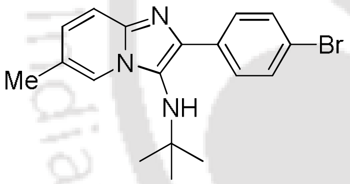
*N-tert-butyl-6-methyl-2-p-tolylH-imidazo[1,2-a]pyridin-3-amine **(21g)***



(21g)

White solid, mp 209-211 °C; **IR** (KBr): 3283, 2967, 2921, 1639, 1557 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): *δ* 7.90 (s, 1H), 7.72 (d, *J* = 7.2 Hz, 2H), 7.36 (d, *J* = 9.2 Hz, 1H), 7.14 (d, *J* = 7.2 Hz, 2H), 6.88 (d, *J* = 9.2 Hz, 1H), 3.04 (bs, NH, 1H), 2.30 (s, 3H), 2.24 (s, 3H), 0.96 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 141.1, 139.4, 137.0, 132.5, 129.0, 128.0, 127.1, 123.1, 121.2, 120.8, 116.6, 56.5, 30.4, 21.4, 18.5. **Anal. Calcd** for $C_{19}H_{23}N_3$ (293.40): C, 77.78; H, 7.90; N, 14.32. Found: C, 77.58; H, 7.82; N, 14.20.

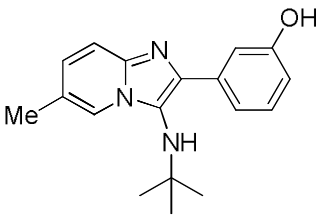
*2-(4-bromophenyl)-N-tert-butyl-6-methylH-imidazo[1,2-a]pyridin-3-amine **(21h)***



(**21h**)

Pale yellow solid, mp 203 °C; **IR** (KBr): 2961, 2925, 2851, 1671 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): *δ* 7.95 (s, 1H), 7.84 (dd, *J* = 8.4 Hz, *J* = 6.4 Hz, 2H), 7.54 (d, *J* = 8.4 Hz, 2H), 7.44 (d, *J* = 8.8 Hz, 1H), 6.99 (dd, *J* = 9.2 Hz, *J* = 1.6 Hz, 1H), 2.34 (s, 3H), 1.22 (bs, NH, 1H), 1.05 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$): 139.7, 136.4, 132.5, 130.3, 128.6, 127.1, 122.4, 120.6, 120.4, 120.1, 115.2, 55.4, 29.4, 17.4. **Anal. Calcd** for $C_{18}H_{20}BrN_3$ (358.27): C, 60.34; H, 5.63; N, 11.73. Found: C, 60.11; H, 5.56; N, 11.62.

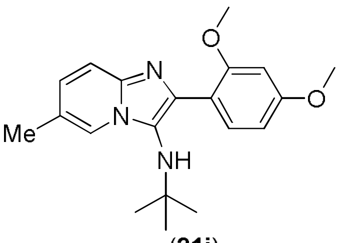
*3-(3-(tert-butylamino)-6-methylH-imidazo[1,2-a] pyridin-2-yl)phenol **(21i)***



(**21i**)

White solid, mp 293 °C; **IR** (KBr): 3445, 2968, 2930, 1596 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): *δ* 7.68 (s, 1H), 7.0-7.05 (m, 3H), 6.81 (t, *J* = 8 Hz, 1H), 6.64 (d, *J* = 8.8 Hz, 1H), 6.37 (dd, *J* = 2.4 Hz, *J* = 2.4 Hz, 1H), 3.2 (bs, 1H, NH), 1.95 (s, 3H), 0.64 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 156.5, 139.6, 137.4, 135.1, 128.5, 127.3, 123.0, 120.8, 120.6, 118.5, 115.1, 114.5, 114.1, 55.6, 29.6, 17.7. **Anal. Calcd** for $C_{18}H_{21}N_3O$ (295.37): C, 73.19; H, 7.17; N, 14.23. Found: C, 73.09; H, 7.10, N, 14.13.

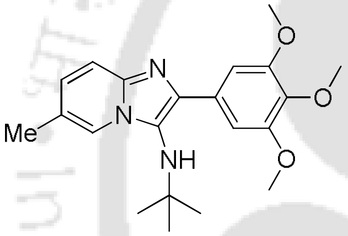
N-tert-butyl-2-(2,4-dimethoxyphenyl)-6-methylH-imidazo[1,2-a]pyridin-3-amine ***(21j)***



(21j)

Yellow semisolid; **IR** (KBr): 2963, 2928, 1611, 1577 cm^{-1}; ^{1}**H NMR** (400 MHz, CDCl$_3$): *δ* 8.11 (s, 1H), 7.77 (d, *J* = 8.8 Hz, 1H), 7.69 (d, *J* = 9.2 Hz, 1H), 7.11 (d, *J* = 9.2 Hz, 1H), 6.66 (dd, *J* = 8.8 Hz, *J* = 2.8 Hz, 1H), 6.52 (d, *J* = 2 Hz, 1H), 3.84 (d, *J* = 7.2 Hz, 6H), 2.35 (s, 3H), 1.22 (bs, NH, 1H), 0.93 (s, 9H); ^{13}**C NMR** (100 MHz, CDCl$_3$): δ 160.3, 156.6, 141.0, 135.7, 131.9, 126.1, 124.8, 120.7, 120.0, 117.6, 115.9, 105.4, 98.6, 55.4, 54.9, 29.6, 29.3, 18.0. **Anal. Calcd** for $C_{20}H_{25}N_3O_2$ (339.43): C, 70.77; H, 7.42; N, 12.38. Found: C, 70.50; H, 7.35; N, 12.28.

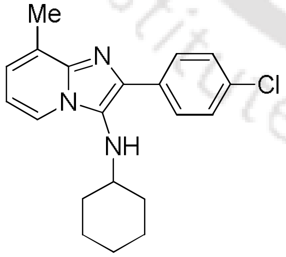
N-tert-butyl-6-methyl-2-(3,4,5-trimethoxyphenyl)H-imidazo[1,2-a]pyridin-3-amine ***(21k)***



(21k)

Yellow semisolid; **IR** (KBr): 2961, 2927, 1586 cm^{-1}; ^{1}**H NMR** (400 MHz, CDCl$_3$): *δ* 7.96 (s, 1H), 7.46 (d, *J* = 8.8 Hz, 2H), 7.0 (d, *J* = 9.2 Hz, 2H), 3.94 (s, 6H), 3.88 (s, 3H), 2.34 (s, 3H), 1.25 (bs, NH, 1H), 1.09 (s, 9H); ^{13}**C NMR** (100 MHz, CDCl$_3$): δ 153.2, 140.6, 138.4, 137.8, 130.2, 128.0, 123.1, 121.6, 121.1, 116.2, 105.6, 61.0, 56.5, 30.6, 29.8, 18.5. **Anal. Calcd** for $C_{21}H_{27}N_3O_3$ (369.45): C, 68.27; H, 7.37; N, 11.37. Found: C, 68.10; H, 7.28; N, 11.26.

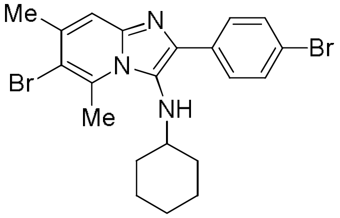
2-(4-chlorophenyl)-N-cyclohexyl-8-methylH-imidazo[1,2-a]pyridin-3-amine ***(21l)***



(21l)

Pale brown solid, mp 108 °C; **IR** (KBr): 2923, 2851, 1634 cm^{-1}; ^{1}**H NMR** (400 MHz, CDCl$_3$): *δ* 8.01 (dd, *J* = 6.8 Hz, *J* = 1.6 Hz, 2H), 7.94 (d, *J* = 6.8 Hz, 1H), 7.40 (dd, *J* = 6.8 Hz, *J* = 2.0 Hz, 2H), 6.92-6.94 (m, 1H), 6.70 (t, *J* = 6.8 Hz, 1H), 3.0 (bs, NH, 1H), 2.90-2.92 (m, 1H), 2.61 (s, 3H), 1.57-1.87 (m, 5H), 1.12-1.25 (m, 5H); ^{13}**C NMR** (100 MHz, CDCl$_3$): δ 142.1, 135.4, 133.5, 132.9, 128.7, 128.6, 127.4, 125.4, 123.0, 120.7, 111.9, 57.0, 34.3, 25.8, 25.0, 16.7. **Anal. Calcd** for $C_{20}H_{22}ClN_3$ (339.86): C, 70.68; H, 6.52; N, 12.36. Found: C, 70.42; H, 6.44; N, 12.29.

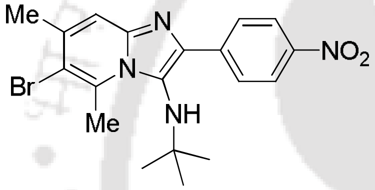
*6-bromo-2-(4-bromophenyl)-N-cyclohexyl-5,7-dimethylH-imidazo[1,2-a]pyridin-3-amine (**21m**)*



(**21m**)

White solid, mp 191 °C; **IR** (KBr): 2928, 2851, 1633 cm^{-1}; ^{1}**H NMR** (400 MHz, CDCl$_3$): δ 7.77 (d, J = 8.8 Hz, 3H), 7.52 (d, J = 8.4 Hz, 2H), 3.45 (s, 3H), 3.14 (s, 3H), 2.68 (bs, NH, 1H), 2.37-2.44 (m, 1H), 1.01-1.72 (m, 10H); ^{13}**C NMR** (100 MHz, CDCl$_3$): δ 142.3, 138.4, 135.5, 134.8, 133.7, 131.5, 129.3, 127.0, 121.5, 114.8, 114.7, 58.6, 33.2, 25.8, 24.9, 24.1, 18.6. **Anal. Calcd** for $C_{21}H_{23}Br_2N_3$ (477.23): C, 52.85; H, 4.86; N, 8.80. Found: C, 52.68; H, 4.79; N, 8.70.

*6-brom-N-tert-butyl-5,7-dimethyl-2-(4-nitrophenyl)H-imidazo[1,2-a]pyridin-3-amine (**21n**)*



(**21n**)

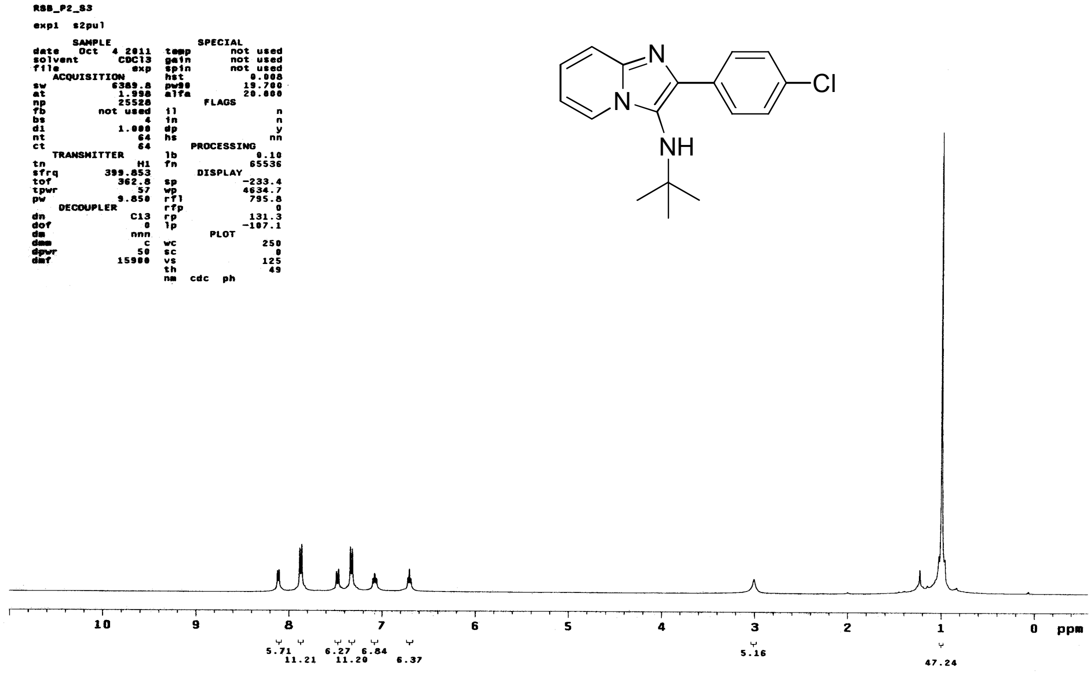
Yellow solid, mp 204-206 °C; **IR** (KBr): 3307, 2963, 1632, 1598 cm^{-1}; ^{1}**H NMR** (400 MHz, CDCl$_3$): δ 8.22 (d, J = 8.4 Hz, 2H), 7.99 (d, J = 8.8 Hz, 3H), 3.18 (bs, NH, 1H), 3.15 (s, 3H), 2.42 (s, 3H), 0.84 (s, 9H); ^{13}**C NMR** (100 MHz, CDCl$_3$): δ 147.0, 142.8, 142.2, 139.8, 136.7, 135.6, 129.2, 127.3, 123.7, 115.8, 115.0, 57.0, 29.7, 24.1, 19.6. **Anal. Calcd** for $C_{19}H_{21}BrN_4O_2$ (417.29): C, 54.69; H, 5.07; N, 13.43. Found: C, 54.45; H, 4.99; N, 13.35.

Complete crystallographic data of **21m** for the structural analyses have been deposited with the Cambridge Crystallographic Data Centre, CCDC No. 848594. Copies of this information may be obtained free of charge from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK, (fax: +44-1223-336033, e-mail: deposit@ccdc.cam.ac.uk or via: www.ccdc.cam.ac.uk).

Table 11. Crystal data and structures refinement for the compound **21m**, for atomic coordinates, equivalent isotropic displacement parameters and bond angles, please check the CIF.

Parameters	Compound **21m**
Empirical Formula	'$C_{21}H_{23}Br_2N_3$'
Formula weight	477.22
Temperature	296 K
CCDC no	848594
Wavelength (Å)	0.71073 Å
Crystal system	Monoclinic
Space group	P 21/c
Radiation type	Mo K\a
Radiation source	'fine-focus sealed tube'
a (Å)	6.3991 (5) Å
b (Å)	32.852 (3) Å
c (Å)	9.1812 (7) Å
α (°)	90.00°
β (°)	90.00°
γ (°)	90.00°
Cell Volume	1930.1 (3) $Å^3$
Z	4
Density	1.639 g/cm^3
F(0 0 0)	956
Index ranges	-6<=h<=7, -39<=k<=39, -11<=l<=10
Number of unique reflections	3480
Number of parameters	237
Number of restraints	0
Goodness-of-fit (GOF)[a] on F^2	4.788
Refinement method	Full-matrix least-squares on F2

***^{1}H NMR (400 MHz, CDCl$_3$)**: N-tert-butyl-2-(4-chlorophenyl)H-imidazo[1,2-a]pyridin-3-amine (21a)*



```
RSB_P2_S3

exp1  s2pul

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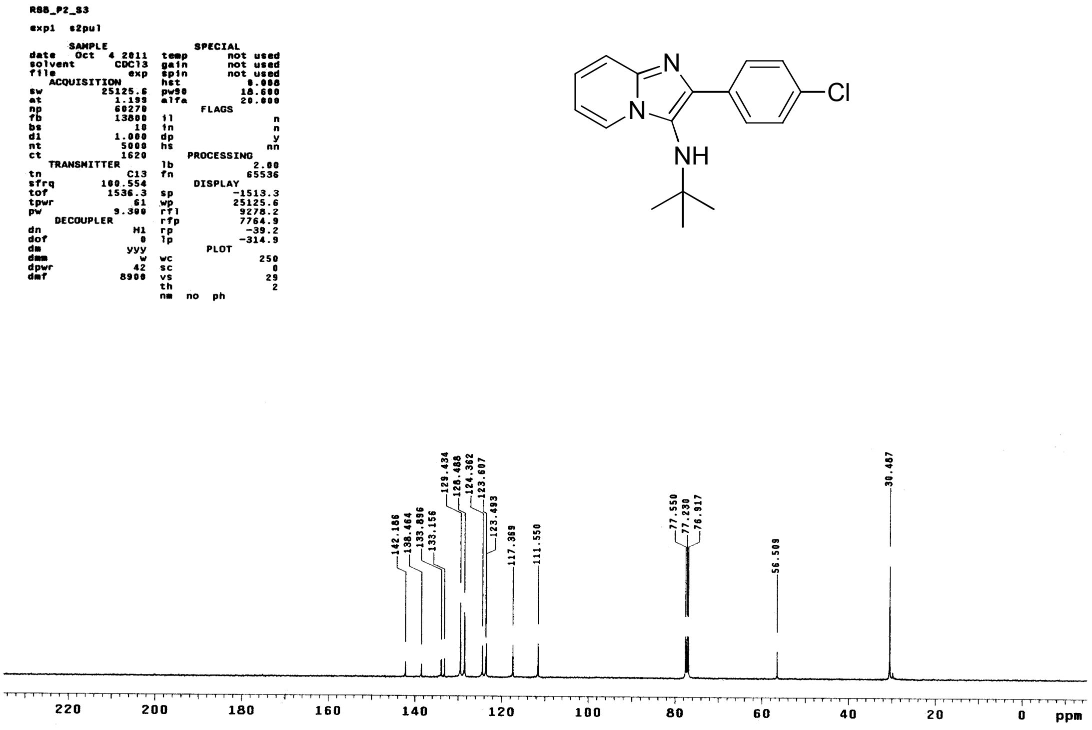
date   Oct  4 2011    temp        not used
solvent       CDCl3   gain        not used
file            exp   spin        not used
   ACQUISITION        hst            0.008
sw           6389.8   pw90          19.700
at            1.998   alfa          20.000
np            25528            FLAGS
fb         not used   il                 n
bs                4   in                 n
d1            1.000   dp                 y
nt               64   hs                nn
ct               64          PROCESSING
   TRANSMITTER        lb              0.10
tn               H1   fn             65536
sfrq        399.853           DISPLAY
tof           362.8   sp            -233.4
tpwr             57   wp            4634.7
pw            9.850   rfl            795.8
    DECOUPLER         rfp                0
dn              C13   rp             131.3
dof               0   lp            -107.1
dm              nnn             PLOT
dmm               c   wc               250
dpwr             50   sc                 0
dmf           15900   vs               125
                      th                49
                      nm   cdc   ph
```

***^{13}C NMR (100 MHz, CDCl$_3$)**: N-tert-butyl-2-(4-chlorophenyl)H-imidazo[1,2-a]pyridin-3-amine (21a)*



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RSB_P2_S3

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solvent       CDCl3   gain        not used
file            exp   spin        not used
   ACQUISITION        hst            0.008
sw          25125.6   pw90          18.600
at            1.199   alfa          20.000
np            60270            FLAGS
fb            13800   il                 n
bs               10   in                 n
d1            1.000   dp                 y
nt             5000   hs                nn
ct             1620          PROCESSING
   TRANSMITTER        lb              2.00
tn              C13   fn             65536
sfrq        100.554           DISPLAY
tof          1536.3   sp           -1513.3
tpwr             61   wp           25125.6
pw            9.300   rfl           9278.2
    DECOUPLER         rfp           7764.9
dn               H1   rp             -39.2
dof               0   lp            -314.9
dm              yyy             PLOT
dmm               w   wc               250
dpwr             42   sc                 0
dmf            8900   vs                29
                      th                 2
                      nm   no   ph
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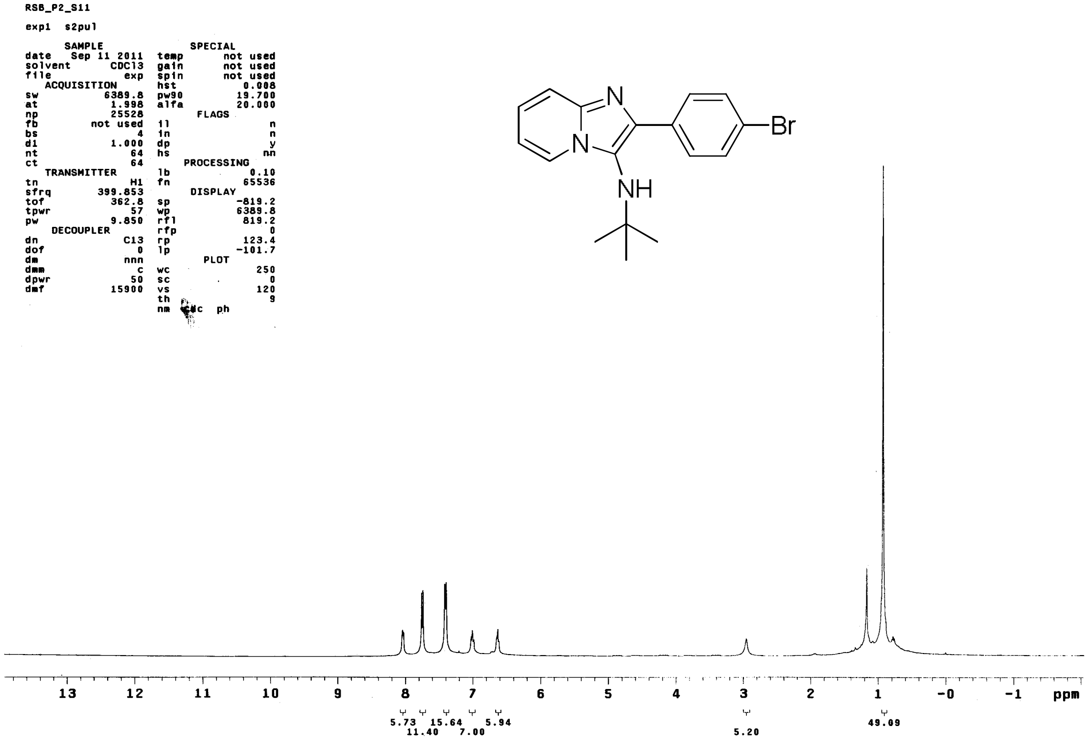
^{1}H NMR (400 MHz, CDCl$_3$)**: 2-(4-bromophenyl)-N-tert-butylH-imidazo[1,2-a]pyridin-3-amine **(21b)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RSB_P2_S11

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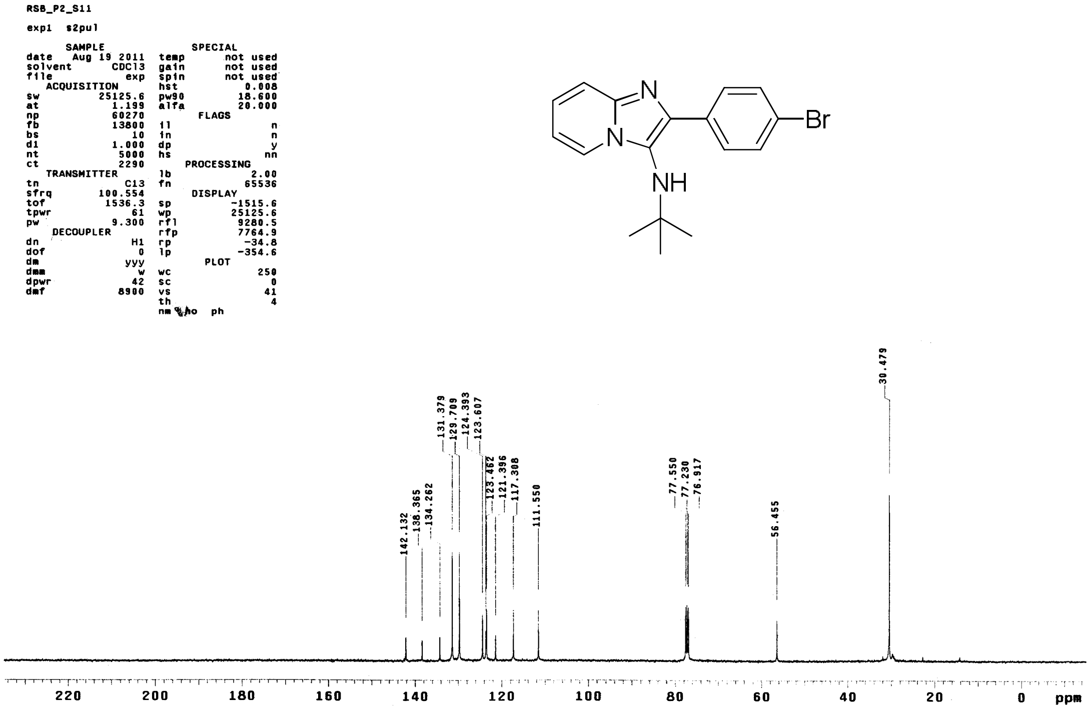
solvent       CDCl3  gain       not used
file            exp  spin       not used
   ACQUISITION       hst           0.008
sw           6389.8  pw90         19.700
at            1.998  alfa         20.000
np            25528          FLAGS
fb         not used  il                n
bs                4  in                n
d1            1.000  dp                y
nt               64  hs               nn
ct               64        PROCESSING
   TRANSMITTER       lb             0.10
tn               H1  fn            65536
sfrq        399.853          DISPLAY
tof           362.8  sp           -819.2
tpwr             57  wp           6389.8
pw            9.850  rfl           819.2
    DECOUPLER        rfp               0
dn              C13  rp            123.4
dof               0  lp           -101.7
dm              nnn           PLOT
dmm               c  wc              250
dpwr             50  sc                0
dmf           15900  vs              120
                     th                9
                     nm [illegible]c  ph
```

^{13}C NMR (100 MHz, CDCl$_3$)**: 2-(4-bromophenyl)-N-tert-butylH-imidazo[1,2-a]pyridin-3-amine **(21b)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RSB_P2_S11

exp1  s2pul

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file            exp  spin       not used
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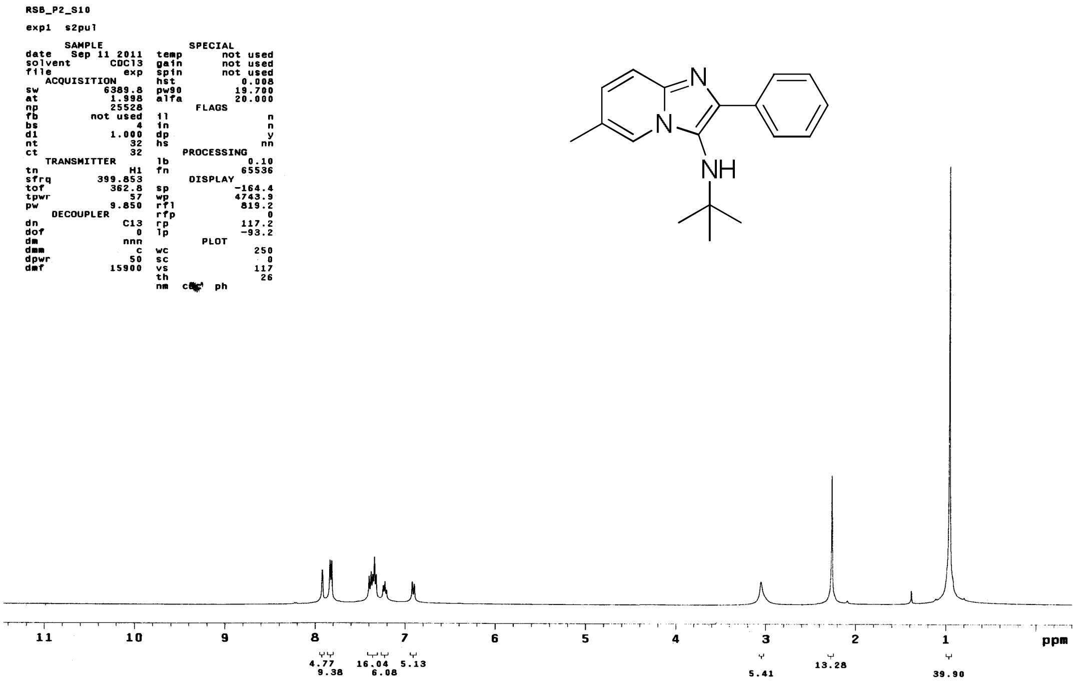
sw          25125.6  pw90         18.600
at            1.199  alfa         20.000
np            60270          FLAGS
fb            13800  il                n
bs               10  in                n
d1            1.000  dp                y
nt             5000  hs               nn
ct             2290        PROCESSING
   TRANSMITTER       lb             2.00
tn              C13  fn            65536
sfrq        100.554          DISPLAY
tof          1536.3  sp          -1515.6
tpwr             61  wp          25125.6
pw            9.300  rfl          9280.5
    DECOUPLER        rfp          7764.9
dn               H1  rp            -34.8
dof               0  lp           -354.6
dm              yyy           PLOT
dmm               w  wc              250
dpwr             42  sc                0
dmf            8900  vs               41
                     th                4
                     nm [illegible]ho  ph
```

^{1}H NMR (400 MHz, CDCl$_3$)**: N-tert-butyl-6-methyl-2-phenylH-imidazo[1,2-a]pyridin-3-amine **(21d)



```
RSB_P2_S10

exp1  s2pul

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solvent      CDCl3  gain       not used
file           exp  spin       not used
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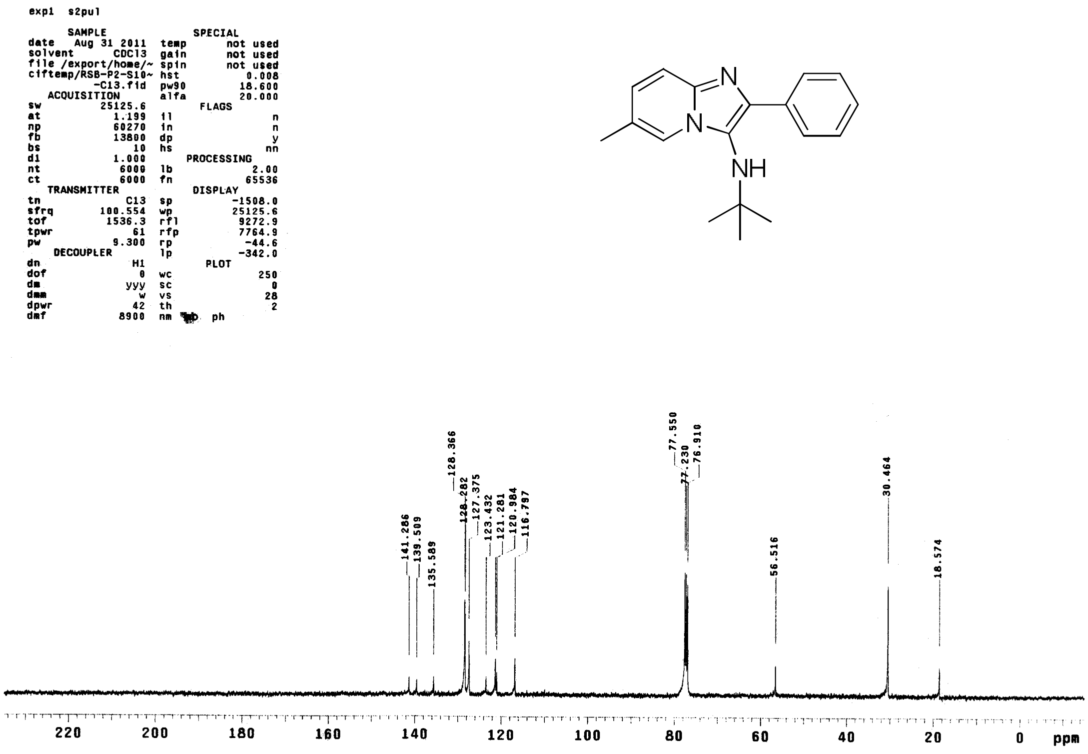
sw          6389.8  pw90         19.700
at           1.998  alfa         20.000
np           25528         FLAGS
fb        not used  il                n
bs               4  in                n
d1           1.000  dp                y
nt              32  hs               nn
ct              32       PROCESSING
   TRANSMITTER      lb             0.10
tn              H1  fn            65536
sfrq       399.853         DISPLAY
tof          362.8  sp           -164.4
tpwr            57  wp           4743.9
pw           9.850  rfl           819.2
    DECOUPLER       rfp               0
dn             C13  rp            117.2
dof              0  lp            -93.2
dm             nnn          PLOT
dmm              c  wc              250
dpwr            50  sc                0
dmf          15900  vs              117
                    th               26
                    nm  c     ph
```

^{13}C NMR (100 MHz, CDCl$_3$)**: N-tert-butyl-6-methyl-2-phenylH-imidazo[1,2-a]pyridin-3-amine **(21d)



```
exp1  s2pul

      SAMPLE              SPECIAL
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solvent      CDCl3  gain       not used
file /export/home/~ spin       not used
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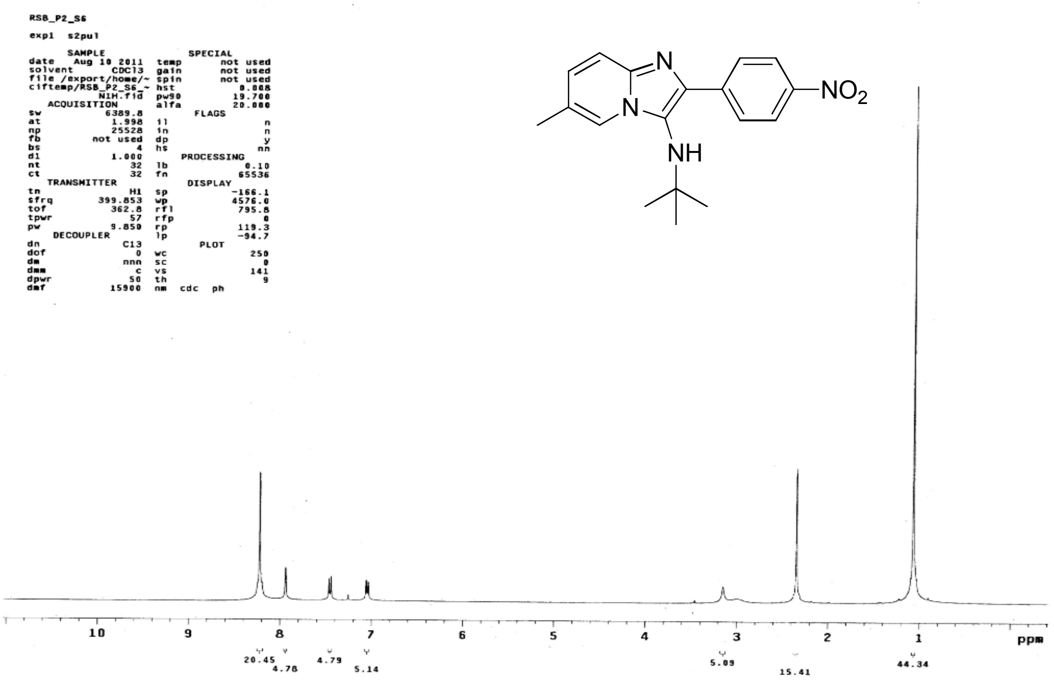
         -C13.fid   pw90         18.600
   ACQUISITION      alfa         20.000
sw         25125.6         FLAGS
at           1.199  il                n
np           60270  in                n
fb           13800  dp                y
bs              10  hs               nn
d1           1.000       PROCESSING
nt            6000  lb             2.00
ct            6000  fn            65536
   TRANSMITTER           DISPLAY
tn             C13  sp          -1508.0
sfrq       100.554  wp          25125.6
tof         1536.3  rfl          9272.9
tpwr            61  rfp          7764.9
pw           9.300  rp            -44.6
    DECOUPLER       lp           -342.0
dn              H1          PLOT
dof              0  wc              250
dm             yyy  sc                0
dmm              w  vs               28
dpwr            42  th                2
dmf           8900  nm        ph
```

***^{1}H NMR (400 MHz, CDCl$_3$)**: N-tert-butyl-6-methyl-2-(4-nitrophenyl)H-imidazo[1,2-a]pyridin-3-amine (**21f**)*



```
RSB_P2_S6

expl  s2pul

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solvent       CDCl3   gain         not used
file /export/home/~   spin         not used
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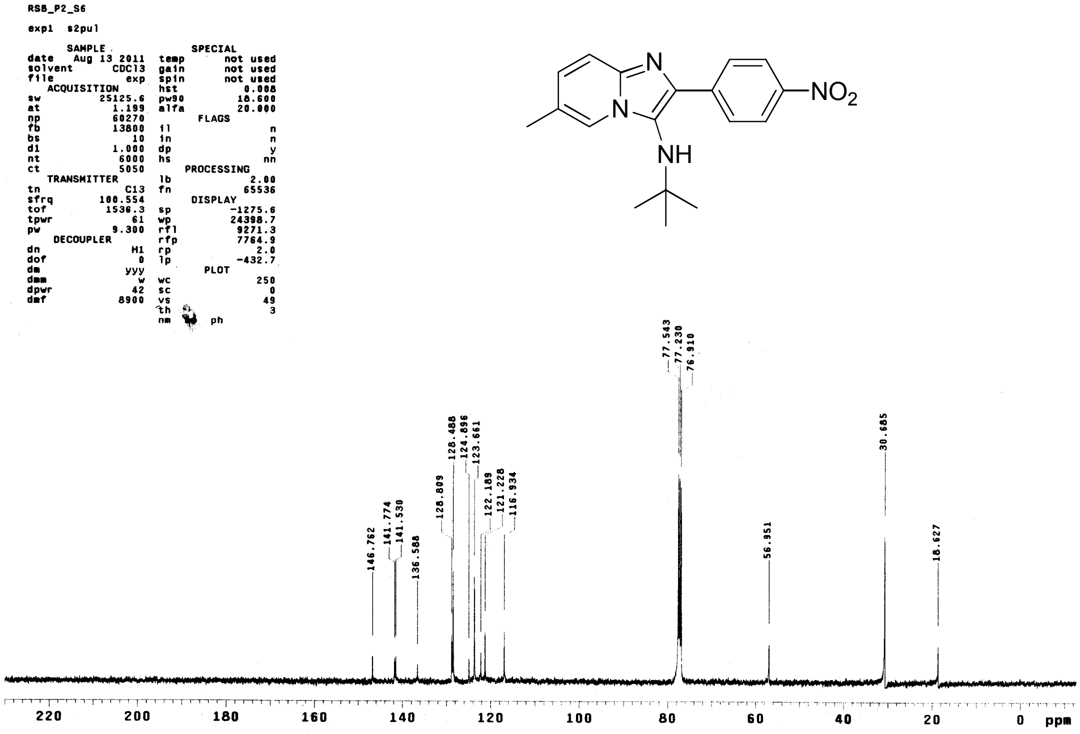
           N1H.fid    pw90           19.700
    ACQUISITION       alfa           20.000
sw           6389.8           FLAGS
at            1.998   il                  n
np            25528   in                  n
fb         not used   dp                  y
bs                4   hs                 nn
d1            1.000        PROCESSING
nt               32   lb               0.10
ct               32   fn              65536
    TRANSMITTER              DISPLAY
tn               H1   sp             -166.1
sfrq        399.853   wp             4576.0
tof           362.8   rfl             795.8
tpwr             57   rfp                 0
pw            9.850   rp              119.3
     DECOUPLER        lp              -94.7
dn              C13            PLOT
dof               0   wc                250
dm              nnn   sc                  0
dmm               c   vs                141
dpwr             50   th                  9
dmf           15900   nm   cdc   ph
```

***^{13}C NMR (100 MHz, CDCl$_3$)**: N-tert-butyl-6-methyl-2-(4-nitrophenyl)H-imidazo[1,2-a]pyridin-3-amine (**21f**)*



```
RSB_P2_S6

expl  s2pul

       SAMPLE                  SPECIAL
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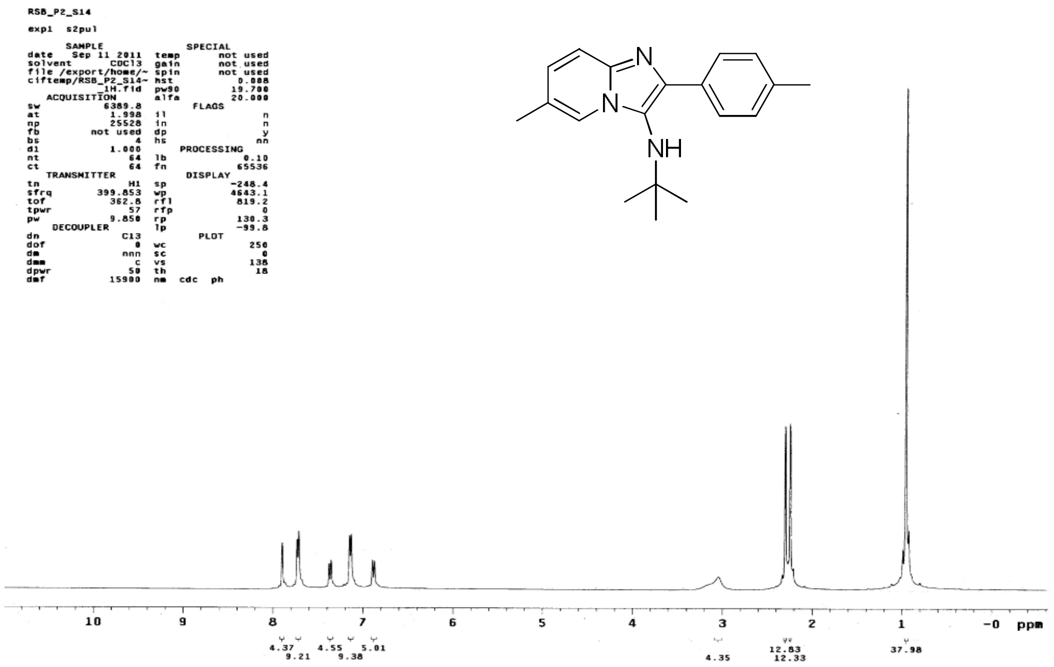
solvent       CDCl3   gain         not used
file            exp   spin         not used
    ACQUISITION       hst             0.008
sw          25125.6   pw90           18.600
at            1.199   alfa           20.000
np            60270           FLAGS
fb            13800   il                  n
bs               10   in                  n
d1            1.000   dp                  y
nt             6000   hs                 nn
ct             5050        PROCESSING
    TRANSMITTER       lb               2.00
tn              C13   fn              65536
sfrq        100.554          DISPLAY
tof          1536.3   sp            -1275.6
tpwr             61   wp            24398.7
pw            9.300   rfl            9271.3
     DECOUPLER        rfp            7764.9
dn               H1   rp                2.0
dof               0   lp             -432.7
dm              yyy            PLOT
dmm               w   wc                250
dpwr             42   sc                  0
dmf            8900   vs                 49
                      th                  3
                      nm        ph
```

^{1}H NMR (400 MHz, CDCl$_3$): *N-tert-butyl-6-methyl-2-p-tolylH-imidazo[1,2-a]pyridin-3-amine* ***(21g)***



```
RSB_P2_S14

exp1  s2pul

      SAMPLE               SPECIAL
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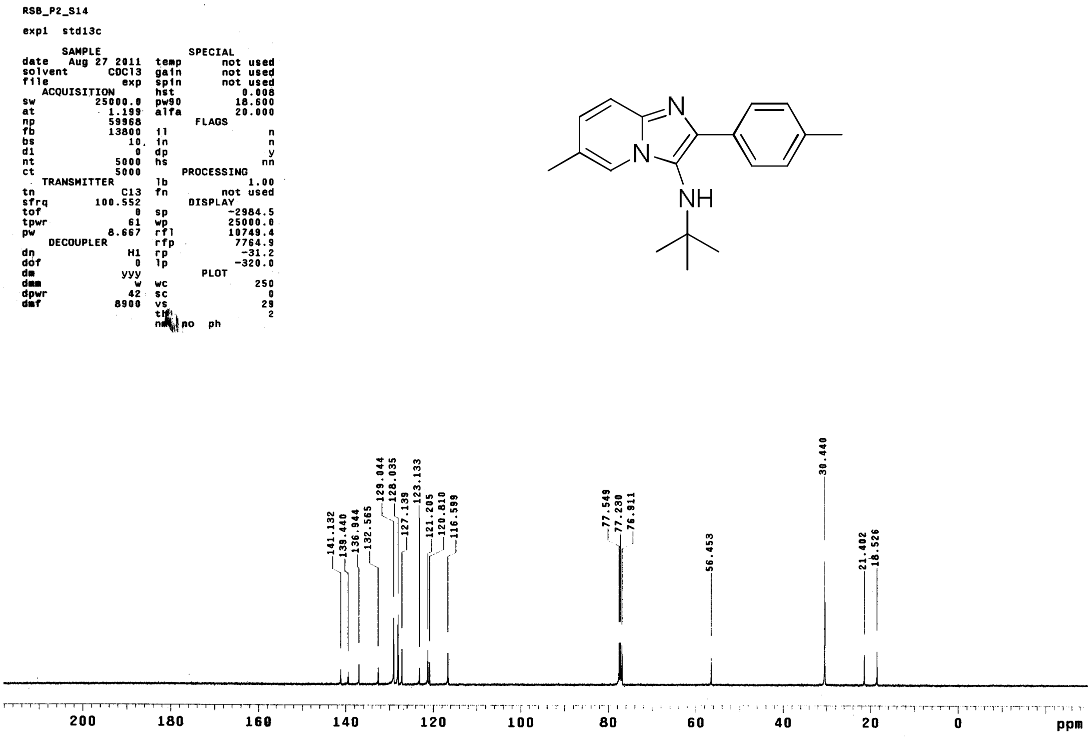
solvent       CDCl3  gain         not used
file /export/home/~ spin         not used
ciftemp/RSB_P2_S14~ hst             0.008
          _1H.fid  pw90           19.700
   ACQUISITION      alfa           20.000
sw           6389.8            FLAGS
at            1.998  il                n
np            25528  in                n
fb         not used  dp                y
bs                4  hs               nn
d1            1.000         PROCESSING
nt               64  lb             0.10
ct               64  fn            65536
   TRANSMITTER               DISPLAY
tn               H1  sp           -248.4
sfrq        399.853  wp           4643.1
tof           362.8  rfl           819.2
tpwr             57  rfp               0
pw            9.850  rp            130.3
    DECOUPLER        lp            -99.8
dn              C13            PLOT
dof               0  wc              250
dm              nnn  sc                0
dmm               c  vs              138
dpwr             50  th               18
dmf           15900  nm  cdc  ph
```

^{13}C NMR (100 MHz, CDCl$_3$): *N-tert-butyl-6-methyl-2-p-tolylH-imidazo[1,2-a]pyridin-3-amine* ***(21g)***



```
RSB_P2_S14

exp1  stdl3c

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solvent       CDCl3  gain       not used
file            exp  spin       not used
   ACQUISITION      hst           0.008
sw          25000.0  pw90         18.600
at            1.199  alfa         20.000
np            59968          FLAGS
fb            13800  il              n
bs               10  in              n
d1                0  dp              y
nt             5000  hs             nn
ct             5000       PROCESSING
   TRANSMITTER      lb             1.00
tn              C13  fn         not used
sfrq        100.552        DISPLAY
tof               0  sp         -2984.5
tpwr             61  wp         25000.0
pw            8.667  rfl        10749.4
    DECOUPLER       rfp          7764.9
dn               H1  rp           -31.2
dof               0  lp          -320.0
dm              yyy           PLOT
dmm               w  wc             250
dpwr             42  sc               0
dmf            8900  vs              29
                     th               2
                     nm  no  ph
```

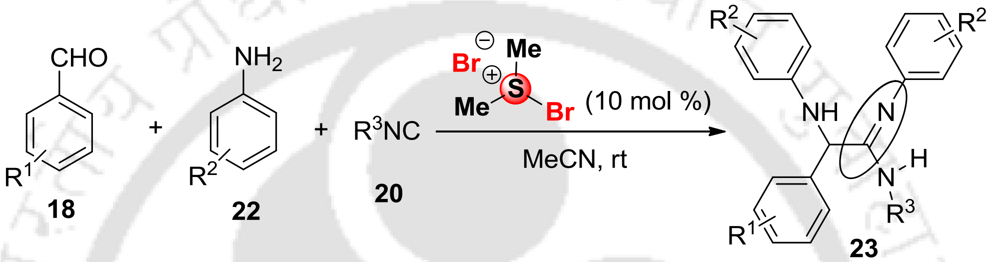
Chapter VI

AB^{2}C type UGI reaction for the Synthesis of α-amino Amidines in presence of Bromodimethylsulfonium bromide (BDMS)

Results and Discussion

Results and Discussion

Brief literature survey of aminoamidine importance and its synthetic paths have been discussed in Chapter IV. To our delight, continuous effort on exploration of BDMS in organic synthesis as a catalyst which access new methodologies to various heterocyclic scaffolds. In this Chapter a new AB^{2}C Ugi reaction is demonstrated for the synthesis of α-amino amidines using aromatic aldehydes, aromatic amines and isocyanides in one-pot three-component reaction catalyzed by bromodimethylsulfonium bromide (BDMS), which is shown in Scheme 72.



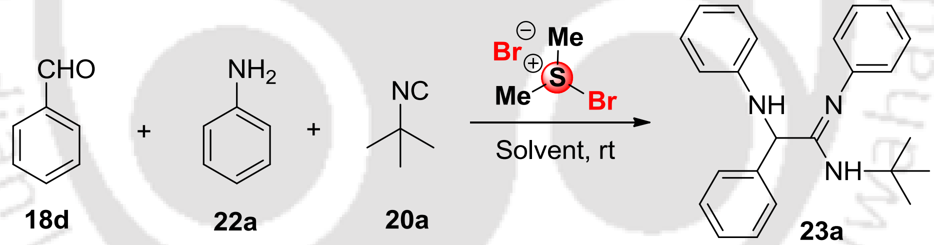
Amines	***Isocyanides***
22a - Aniline	***20a*** - *tert*-butyl
22b - 4-Chloroaniline	***20b*** - Cyclohexyl
22c - 4-bromoaniline	***20c*** - 2-Morpholinoethyl
22d - 3,4-dimethylaniline	

Scheme 72. Synthesis of α-amino amidine using three-component reaction

Bromodimethylsulfonium bromide (BDMS) is found to be a cheap and readily available catalyst used for various organic transformations. Our initial effort began from the preparation of the catalyst BDMS by known literature procedure followed by optimization of the reaction condition by using benzaldehyde (**18d**), aniline (**22a**) and *tert*-butyl isocyanide (**20a**) as a model substrate. Various reactions were scrutinized with different mol % of the catalyst and with different solvent such as CH_2Cl_2, CH_3CN and MeOH. Initial attempts were carried out on reaction with 2 mol %, 4 mol %, and 5 mol % of BDMS which provided 57%, 61% and 68% yield, respectively (Table 12, entries 4-6). Meanwhile, in case of 10 mol% of BDMS, the reaction underwent smoothly and it also enhances the yield to 92% (Table 12, entry 7). We also observe that the reaction did not take place in absence of catalyst. From this point, it was clear that BDMS plays a major role for the synthesis of α-amino amidine. However, it was noted that excess loading of the catalyst BDMS decreased the yield (Table 12, entry 8). The output of the optimized results indicates that 10 mol% of BDMS is sufficient for the synthesis of α-amino amidine.

We sought to study the solvent role by executing the same reaction with different solvent such as dichloromethane, acetonitrile and methanol. However, acetonitrile was found to be the best solvent for this synthesis. Eventually, the isolated product **23a** was characterized by ^{1}H NMR which indicated a singlet for tertiary butyl proton at 1.46, –CH proton as singlet at 4.92, –NH proton as two broad peak at 3.71, 5.90 and aromatic proton at 6.48-7.30 ppm respectively. On the other hand, the peak at 154 ppm in ^{13}C NMR corresponds to C=N of α-amino amidine **23a**. Moreover, the structure of α-amino amidine derivative **23a** was confirmed through single-X-ray crystallographic data as shown in Figure 11. Each unit cell contained four molecule of **23a** embedded in the crystal lattice in $P2_1/c$ space group. The analysis of the crystal structure specify the position of the C=N (C7−N1 = 1.27 Å) and the protonated nitrogen attached to the alkyl group (C7−N3 = 1.36 Å).

Table 12. Optimization of reaction condition for the synthesis of α-amino amidine **23a**[a]



Entry	BDMS used	Solvent	Time (h)	Yield (%)[b]
1	-	CH_2Cl_2	22	00
2	2 mol%	CH_2Cl_2	7	52
3	2 mol%	CH_3OH	6	45
4	2 mol%	CH_3CN	5	57
5	4 mol%	CH_3CN	4	61
6	5 mol%	CH_3CN	3	68
7	10 mol%	CH_3CN	1	92
8	15 mol%	CH_3CN	2	91

[a] The reactions were performed using 1mmol of benzaldehyde (**18d**), 2 mmol of aniline (**22a**), 1 mmol of *tert*-butyl isocyanide (**20a**) in 5 mL of solvent at room temperature.
[b] Isolated yield.

The optimized protocol was further explored with various aromatic aldehydes, substituted aromatic amines and isocyanides which afford the resulting product of α-amino amidine derivatives in good yields as depicted in Table 13. We notice that **23q** offer a low yield of the product (Table 13, entry 17) due to less reactivity of 2-morpholinoethyl isocyanide. The respective products of all α-amino amidine derivatives were characterized by ^{1}H-NMR, ^{13}C-NMR and elemental analysis. To our delight, next the reaction were performed with benzaldehyde (**18d**), aniline (**22a**) and *tert*-butyl isocyanide (**20a**) using 48% aqueous HBr at room temperature in order to compare the effectiveness of BDMS. However it resulted in a low yield of **23a** with 40% after 4h.

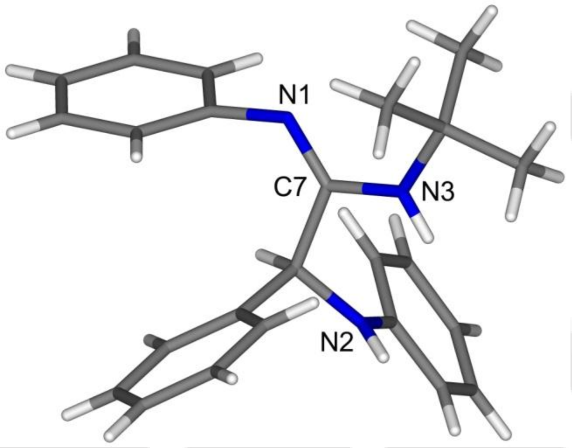
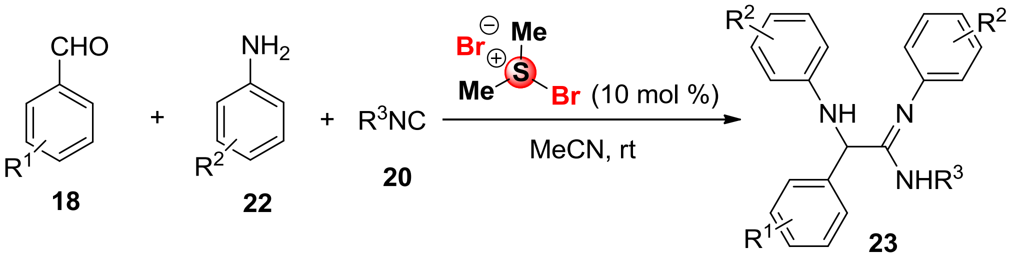
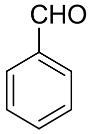
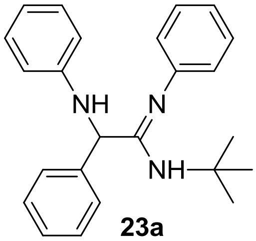
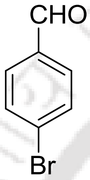
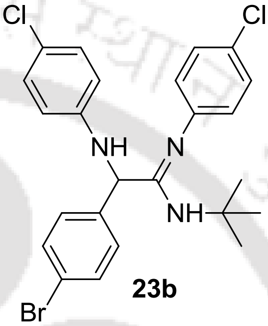
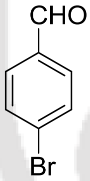
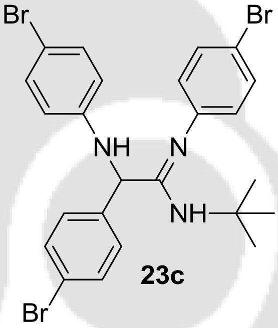
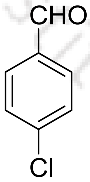
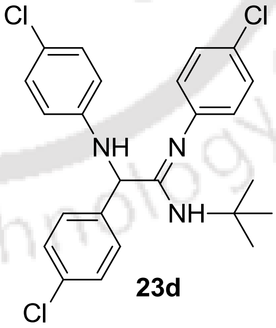
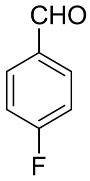
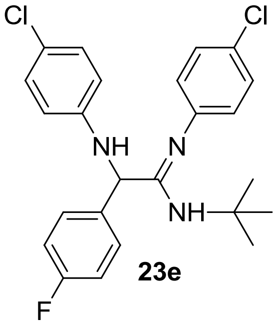


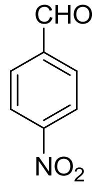
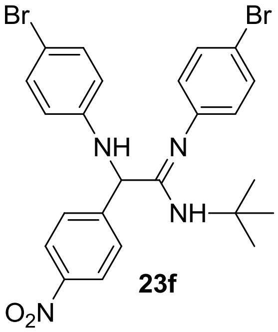
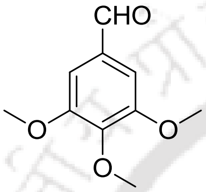
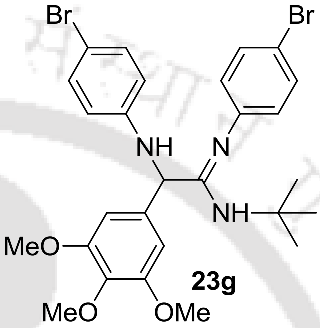
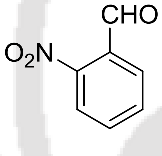
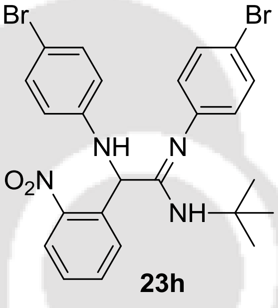
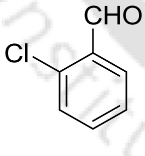
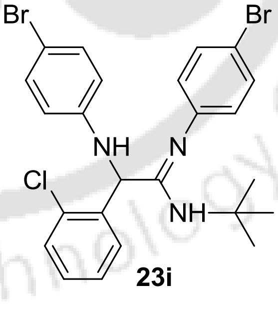
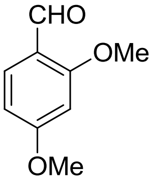
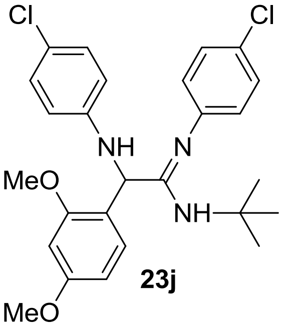
Figure 11. Crystal structures of **23a**

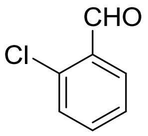
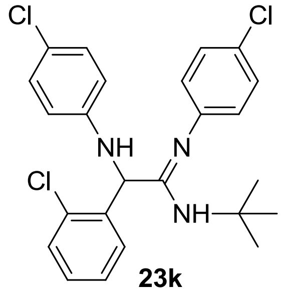
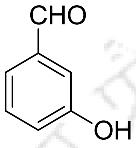
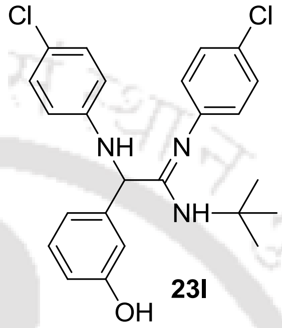
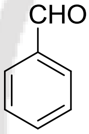
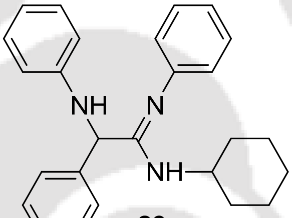
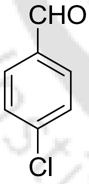
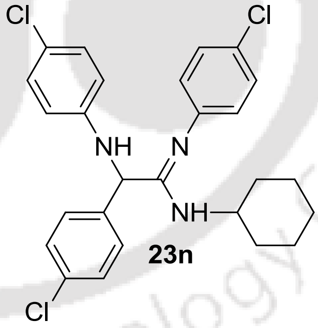
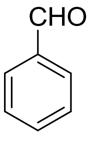
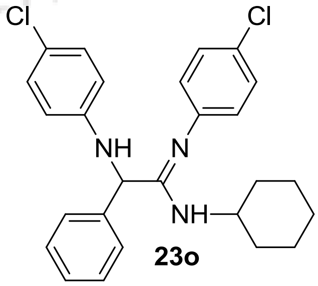
In addition, the structure of the molecule **23b** and **23n** was also determined by single-crystal X-ray crystallography data. The compounds **23b** and **23n** are isostructural to **23a** and the protonated nitrogen attached to the alkyl group (C25−N1 = 1.35 Å in **23b** and C14−N3 = 1.34 Å in **23n**) is shown in Figure 12a and 12b.

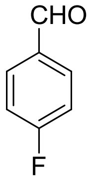
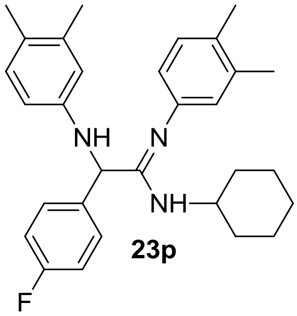
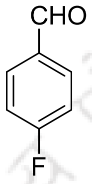
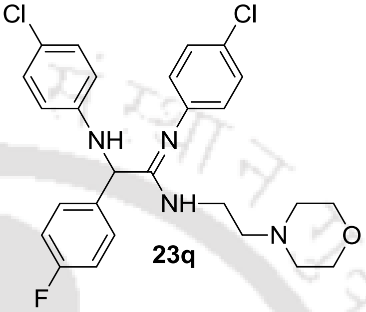
Table 13. BDMS-catalyzed synthesis of α-amino amidines[a]



S.No	Aldehyde (**18**)	Amine (**22**)	R^3NC (**20**)	Product (**23**)	Time (h)	Yield (%)[b]
1	 **18d**	**22a**	**20a**	 **23a**	1	92
2	 **18b**	**22b**	**20a**	 **23b**	1	85
3	 **18b**	**22c**	**20a**	 **23c**	2.5	77
4	 **18a**	**22b**	**20a**	 **23d**	0.5	93
5	 **18k**	**22b**	**20a**	 **23e**	1.5	89

6	 **18f**	**22c**	**20a**	 **23f**	2.5	76
7	 **18i**	**22c**	**20a**	 **23g**	3	82
8	 **18l**	**22c**	**20a**	 **23h**	2	75
9	 **18m**	**22c**	**20a**	 **23i**	3	65
10	 **18h**	**22b**	**20a**	 **23j**	3.5	78

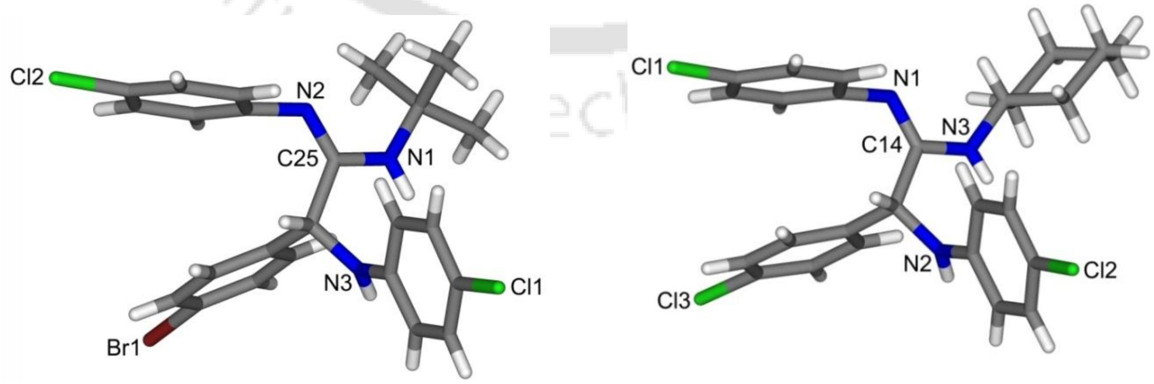
11	 **18m**	**22b**	**20a**	 **23k**	1	87
12	 **18c**	**22b**	**20a**	 **23l**	2	82
13	 **18d**	**22a**	**20b**	 **23m**	1.5	85
14	 **18a**	**22b**	**20b**	 **23n**	0.5	90
15	 **18d**	**22b**	**20b**	 **23o**	3.5	80

16	 **18k**	**22d**	**20b**	 **23p**	4	76
17	 **18k**	**22b**	**20c**	 **23q**	6	35

[a]All the reactions were carried out using 1 mmol of aldehyde, 2 mmol of amine and 1 mmol of isocyanide in 5 mL acetonitrile at room temperature. [b]Isolated yield.

Interestingly, the inter-molecular hydrogen bonding interactions in **23n** through N−H···N bonds (H···N = 2.24 Å, N···N = 3.074 Å, ∠N−H···N = 164°) propagated along *b*-axis which exhibited a one-dimension zigzag structure as depicted in Figure 13.

The plausible mechanism of α-amino amidine can be elucidated as follows: In the first step the aromatic amine reacts with aromatic aldehyde to form imine **1a** and water. The liberated water molecule reacts with BDMS which leads to the formation of dimethyl sulfide, HOBr and HBr. Then the imine **1a** undergoes protonation with the liberated HBr to form **1b**, which reacts with isocyanide to form intermediate **1c**.



(a) **(b)**

Figure 12. Molecular structure of (a) **23b** and (b) **23n**

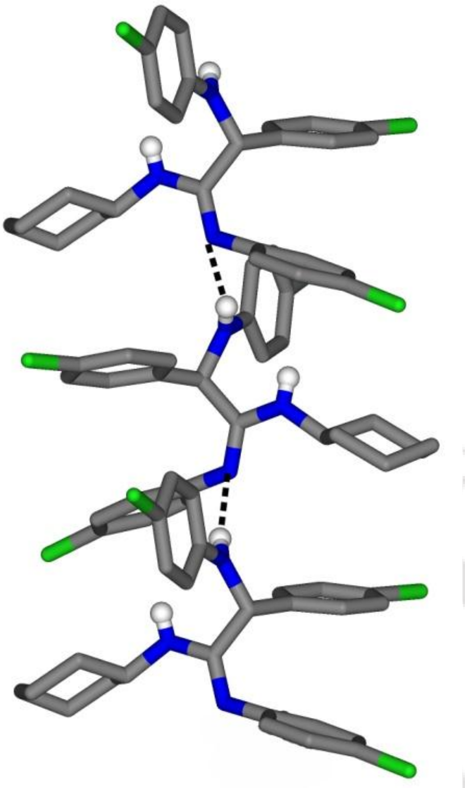
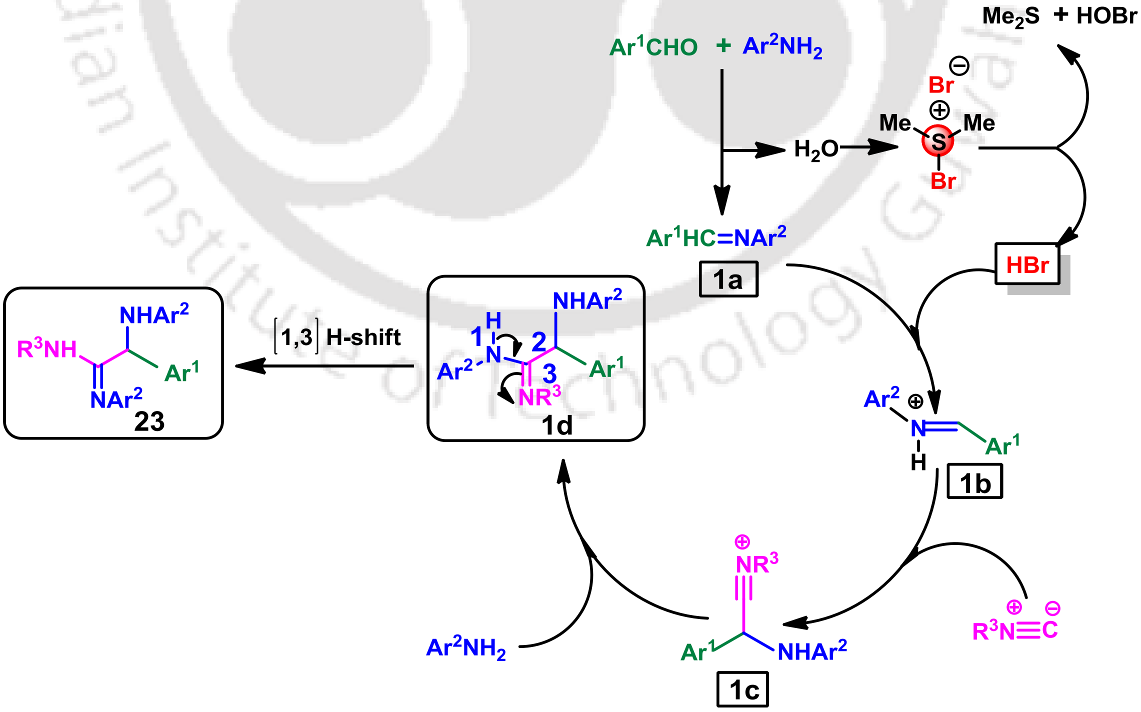


Figure 13. Zigzag hydrogen bonded chain of **23n** propagated along *b*-axis



Scheme 73. Plausible Mechanism for the formation of α-aminoamidine

The intermediate **1c** further reacts with another molecule of amine to give α-amino amidines **1d** which undergoes [1,3] hydrogen shift to afford the product of α-amino amidines **23** as shown in Scheme 73.

In conclusion, we have developed a new one-pot three-component AB^{2}C type UGI reaction for the synthesis of α-amino amidines using aromatic aldehydes, aromatic amines and isocyanides in presence of bromodimethylsulfonium bromide (BDMS) as a catalyst. The important aspects of the present protocol are metal-free catalyst, good yield, shorter reaction time, and variety of substrate scope compatibility, mild reaction conditions, easy separation and purification process. In addition to that, the molecule **23n** forms fascinating one-dimension zigzag structure via inter-molecular hydrogen bonding interactions.

Experimental Section

AB^{2}C type UGI reaction for the Synthesis of α-amino Amidines in presence of Bromodimethylsulfonium bromide (BDMS)

Chapter VI

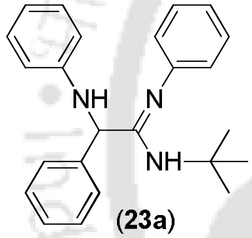
Experimental Section

General procedure for the synthesis of a-amino amidine

To a stirred mixture of aromatic aldehyde (1 mmol), aromatic amine (2 mmol) and isocyanide (1 mmol) in 5 mL acetonitrile, a catalytic amount of bromodimethyl sulfonium bromide (0.022 g) was added at room temperature and allowed to stir till the completion of reaction as indicated by TLC. Then, the reaction mixture was concentrate in a rotary evaporator and the obtained residue was treated with 5 mL methanol, a crystalline product separate out, which was filtered off and washed with cold methanol, diethyl ether and finally dried under reduced pressure.

Spectral data of Compounds

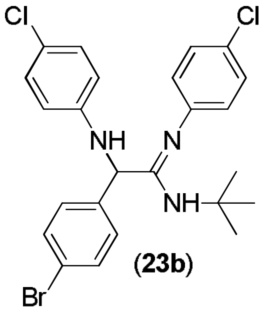
N-tert-Butyl-N',2-diphenyl-2-(phenyl amino)acetamidine (**23a**)



(23a)

White solid, mp 134 °C; **IR** (KBr): 3389, 3027, 2963, 2906, 1634, 1601, 1591, 1485, 1310, 1253, 1220, 1185, 1166, 1070 cm^{-1}; ^{1}**H NMR** (400 MHz, CDCl$_3$): δ 7.30-7.22 (m, 5H), 7.14 (dd, *J* = 8 Hz, *J* = 2 Hz, 2H), 7.03 (t, *J* = 8 Hz, 2H), 6.86-6.81 (m, 2H), 6.70 (d, *J* = 7.6 Hz, 2H), 6.48 (d, *J* = 7.2 Hz, 2H), 5.90 (bs, 1H, NH), 4.92 (s, 1H), 3.71 (bs, 1H, NH), 1.46 (s, 9H); ^{13}**C NMR** (100 MHz, CDCl$_3$): δ 154.0, 150.7, 147.3, 140.0, 129.4, 128.9, 128.6, 128.4, 128.2, 122.4, 121.3, 119.5, 113.9, 60.0, 51.0, 28.5. **Anal. Calcd** for $C_{24}H_{27}N_3$ (357.49): C, 80.63; H, 7.61; N, 11.75. Found: C, 80.54; H, 7.53; N, 11.66.

2-(4-Chlorophenylamino)-N-tert-butyl-2-(4-bromophenyl)-N'-(4-chlorophenyl)acetamidine (**23b**)

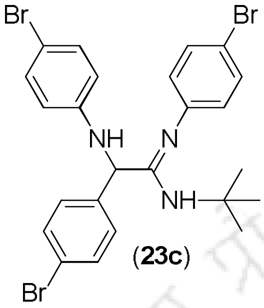


(23b)

Pale yellow solid, mp 190 °C; **IR** (KBr): 3382, 2963, 1640, 1485, 1259, 1084 cm^{-1}; ^{1}**H NMR** (400 MHz, CDCl$_3$): δ 7.44 (d, *J* = 8.4 Hz, 2H), 7.19 (d, *J* = 8.8 Hz, 2H), 7.03 (dd, *J* = 8.8 Hz, *J* = 4.0 Hz, 4H), 6.57 (d, *J* = 8.8 Hz, 2H), 6.38 (d, *J* = 8.4 Hz, 2H), 5.79 (bs, 1H, NH), 4.79 (s, 1H), 3.68 (bs, 1H, NH), 1.43 (s, 9H); ^{13}**C NMR** (100 MHz, CDCl$_3$): δ 153.5, 149.1, 145.3, 138.3, 135.1, 132.4, 129.8, 129.5, 128.8, 126.7, 124.8, 123.5, 115.0, 59.4, 51.4, 28.5. **Anal. Calcd** for $C_{24}H_{24}BrCl_2N_3$ (505.28): C, 57.05; H, 4.79; N, 8.32. Found: C,

56.92; H, 4.70; N, 8.21. **HRMS** (ESI) calcd for $C_{24}H_{24}BrCl_2N_3$ [M+H] 506.0581 found 506.0600.

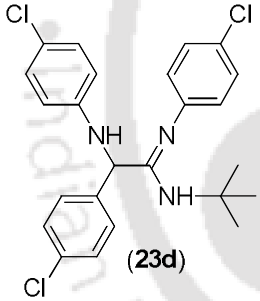
2-(4-Bromophenylamino)-N-tert-butyl-N',2-bis(4-bromophenyl)acetamidine (**23c**)



(**23c**)

Pale yellow solid, mp 182 °C; **IR** (KBr): 3381, 2965, 2901, 1641, 1591, 1581, 1506, 1488, 1388, 1253, 1180, 1164, 1070 cm^{-1}; ^{1}**H NMR** (400 MHz, $CDCl_3$): δ 7.43 (d, *J* = 8.4 Hz, 2H), 7.32 (d, *J* = 8.4 Hz, 2H), 7.16 (d, *J* = 8.0 Hz, 2H), 7.02 (d, *J* = 8.0 Hz, 2H), 6.52 (d, *J* = 8.8 Hz, 2H), 6.33 (d, *J* = 8.4 Hz, 2H), 5.77 (bs, 1H, NH), 4.78 (s, 1H), 3.71 (bs, 1H, NH), 1.42 (s, 9H); ^{13}**C NMR** (100 MHz, $CDCl_3$): δ 153.4, 149.5, 145.7, 138.2, 132.4, 131.7, 129.8, 124.0, 122.9, 115.4, 114.3, 111.9, 59.3, 51.4, 28.4. **Anal. Calcd** for $C_{24}H_{24}Br_3N_3$ (594.18): C, 48.51; H, 4.07; N, 7.07. Found: C, 48.42; H, 3.98; N, 6.97.

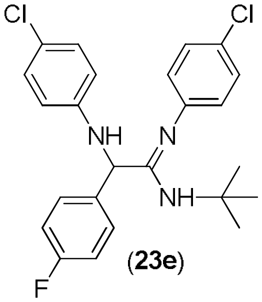
2-(4-Chlorophenylamino)-N-tert-butyl-N',2-bis(4-chlorophenyl)acetamidine (**23d**)



(**23d**)

White solid, mp 180 °C; **IR** (KBr): 3384, 2967, 2901, 1641, 1491, 1482, 1284, 1253, 1180, 1088 cm^{-1}; ^{1}**H NMR** (400 MHz, $CDCl_3$): δ 7.28 (d, *J* = 8.4 Hz, 2H), 7.19 (d, *J* = 8.8 Hz, 2H), 7.08 (d, *J* = 8.4 Hz, 2H), 7.03 (d, *J* = 8.4 Hz, 2H), 6.57 (d, *J* = 8.8 Hz, 2H), 6.38 (d, *J* = 8.4 Hz, 2H), 5.80 (bs, 1H, NH), 4.80 (s, 1H), 3.68 (bs, 1H, NH), 1.43 (s, 9H); ^{13}**C NMR** (100 MHz, $CDCl_3$): δ 153.6, 149.1, 145.4, 137.8, 134.8, 129.6, 129.5, 129.4, 128.8, 126.7, 124.8, 123.6, 115.0, 59.4, 51.4, 28.5. **Anal. Calcd** for $C_{24}H_{24}Cl_3N_3$ (460.83): C, 62.55; H, 5.25; N, 9.12. Found: C, 62.44; H, 5.17; N, 9.02.

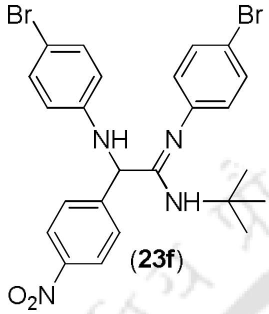
2-(4-Chlorophenylamino)-N-tert-butyl-N'-(4-chlorophenyl)-2-(4-fluorophenyl)acetamidine (**23e**)



(**23e**)

White solid, mp 153 °C; **IR** (KBr): 3408, 3386, 2964, 2924, 1634, 1601, 1509, 1494, 1483, 1230, 1181, 1157, 1086 cm^{-1}; ^{1}**H NMR** (400 MHz, $CDCl_3$): δ 7.19 (d, *J* = 9.2 Hz, 2H), 7.25-7.10 (m, 2H), 7.03-6.97 (m, 4H), 6.58 (d, *J* = 8.8 Hz, 2H), 6.37 (d, *J* = 8.8 Hz, 2H), 5.83 (bs, 1H, NH), 4.80 (d, *J* = 1.6 Hz, 1H), 3.69 (bs, 1H, NH), 1.43 (s, 9H); ^{13}**C NMR** (100 MHz, $CDCl_3$): δ 153.9, 149.1, 145.5, 135.1, 130.0, 129.5, 128.7, 126.6, 124.7, 123.5, 116.2, 116.0, 115.0, 59.4, 51.3, 28.5. **Anal. Calcd** for $C_{24}H_{24}Cl_2FN_3$ (444.37): C, 64.87; H, 5.44; N, 9.46. Found: C, 64.76; H, 5.38; N, 9.34.

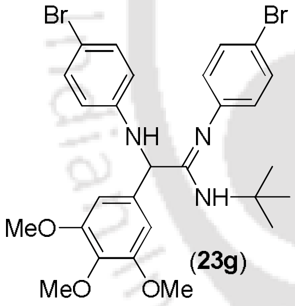
2-(4-Bromophenylamino)-N-tert-butyl-N'-(4-bromophenyl)-2-(4-nitrophenyl)acetamidine (**23f**)



(**23f**)

Yellow solid, mp 218 °C; **IR** (KBr): 3384, 2960, 1634, 1522, 1492, 1479, 1347, 1182 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.17 (d, *J* = 8.8 Hz, 2H), 7.37-7.32 (m, 4H), 7.18 (d, *J* = 8.4 Hz, 2H), 6.55 (d, *J* = 8.8 Hz, 2H), 6.33 (d, *J* = 8.8 Hz, 2H), 5.77 (bs, 1H, NH), 4.99 (d, *J* = 1.6 Hz, 1H), 3.73 (bs, 1H, NH), 1.44 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 152.7, 149.3, 148.0, 145.9, 145.4, 132.5, 131.9, 129.3, 124.4, 123.8, 115.6, 114.6, 112.4, 59.2, 51.6, 28.4. **Anal. Calcd** for $C_{24}H_{24}Br_2N_4O_2$ (560.28): C, 51.45; H, 4.32; N, 10.00. Found: C, 51.32; H, 4.26; N, 9.90.

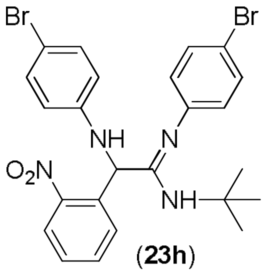
2-(4-Bromophenylamino)-N-tert-butyl-N'-(4-bromophenyl)-2-(3,4,5-trimethoxyphenyl) acetamidine (**23g**)



(**23g**)

White solid, mp 215 °C; **IR** (KBr): 3382, 3362, 2958, 2935, 1637, 1595, 1508, 1481, 1329, 1131 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.34 (d, *J* = 8.4 Hz, 2H), 7.17 (d, *J* = 8.8 Hz, 2H), 6.54 (d, *J* = 8.8 Hz, 2H), 6.36 (d, *J* = 8.4 Hz, 2H), 6.32 (s, 2H), 5.89 (bs, 1H, NH), 4.71 (s, 1H), 3.85 (s, 3H), 3.76 (s, 7H), 1.44 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 153.9, 153.6, 149.9, 146.1, 138.3, 134.6, 132.4, 131.6, 124.3, 115.5, 114.1, 111.8, 105.1, 61.2, 60.5, 56.3, 51.3, 28.6. **Anal. Calcd** for $C_{27}H_{31}Br_2N_3O_3$ (605.36): C, 53.57; H, 5.16; N, 6.94. Found: C, 53.42; H, 5.08; N, 6.85.

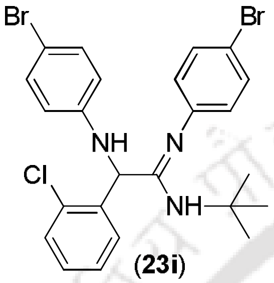
2-(4-Bromophenylamino)-N-tert-butyl-N'-(4-bromophenyl)-2-(2-nitrophenyl)acetamidine (**23h**)



(**23h**)

Light yellow solid, mp 198 °C; **IR** (KBr): 3357, 3298, 2969, 2956, 1615, 1580, 1520, 1480, 1347, 1258, 1181, 1071 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.75 (d, *J* = 8.8 Hz, 1H), 7.61-7.60 (m, 2H), 7.50-7.45 (m, 1H), 7.34 (d, *J* = 8.8 Hz, 2H), 7.06 (d, *J* = 8.8 Hz, 2H), 6.55 (d, *J* = 8.8 Hz, 2H), 6.16 (d, *J* = 8.8 Hz, 2H), 5.98 (bs, 1H, NH), 5.34 (d, *J* = 3.2 Hz, 1H), 3.94 (bs, 1H, NH), 1.45 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 153.4, 149.3, 149.0, 145.8, 133.7, 133.0, 132.4, 131.7, 130.0, 129.8, 125.0, 123.4, 115.7, 114.4, 112.3, 56.1, 51.6, 28.4. **Anal. Calcd** for $C_{24}H_{24}Br_2N_4O_2$ (560.28): C, 51.45; H, 4.32; N, 10.00. Found: C, 51.34; H, 4.25; N, 9.90.

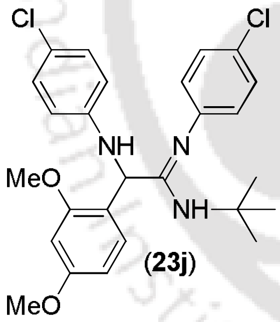
N'-(4-Bromophenyl)-2-(4-bromophenylamino)-N-tert-butyl-2-(2-chlorophenyl)acetamidine (**23i**)



(23i)

White solid, mp 166 °C; **IR** (KBr): 3373, 2966, 1719, 1669, 1633, 1588, 1492, 1373, 1212, 1127, 1071, 1033 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.57 (d, *J* = 6.4 Hz, 1H), 7.34-7.29 (m, 5H), 7.11 (d, *J* = 8.8 Hz, 2H), 6.54 (d, *J* = 8.8 Hz, 2H), 6.27 (d, *J* = 8.8 Hz, 2H), 5.89 (bs, 1H, NH), 5.16 (s, 1H), 3.65 (bs, 1H, NH), 1.47 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 153.7, 149.6, 146.3, 136.7, 134.9, 132.3, 131.8, 131.6, 130.2, 129.1, 127.4, 123.6, 115.4, 114.2, 111.9, 57.1, 51.4, 28.5. **Anal. Calcd** for $C_{24}H_{24}Br_2ClN_3$ (549.73): C, 52.44; H, 4.40; N, 7.64. Found: C, 52.38; H, 4.28; N, 7.52.

2-(4-Chlorophenylamino)-N-tert-butyl-N'-(4-chlorophenyl)-2-(2,4dimethoxyphenyl)acetamidine (**23j**)

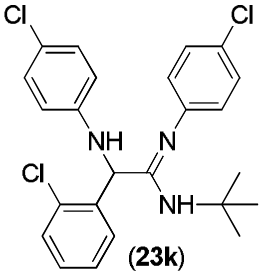


(23j)

White solid, mp 140 °C; **IR** (KBr): 3358, 2962, 2838, 1614, 1587, 1509, 1493, 1482, 1290, 1207, 1171, 1098, 1032 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.30 (d, *J* = 8.4 Hz, 1H), 7.17 (d, *J* = 8.8 Hz, 2H), 6.96 (d, *J* = 8.8 Hz, 2H), 6.56 (d, *J* = 9.2 Hz, 2H), 6.47 (dd, *J* = 8.4 Hz, *J* = 2.4 Hz, 1H), 6.33 (d, *J* = 8.4 Hz, 2H), 6.28 (d, *J* = 2 Hz, 1H), 5.92 (bs, 1H, NH), 5.05 (s, 1H), 3.82 (s, 3H), 3.64 (bs, 1H, NH), 3.42 (s, 3H), 1.44 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 161.3, 158.0, 155.3, 149.8, 146.3, 129.2, 129.0, 128.3, 126.0, 124.0, 123.6, 120.1, 115.0, 104.6, 98.5, 55.5, 55.4, 53.4, 51.1, 28.5. **Anal. Calcd** for $C_{26}H_{29}Cl_2N_3O_2$ (486.43): C, 64.20; H, 6.01; N, 8.64. Found: C, 64.08; H, 5.93; N, 8.56.

2-(4-Chlorophenylamino)-N-tert-butyl-2-(2-chlorophenyl)-N'-(4-chlorophenyl)acetamidine (**23k**)

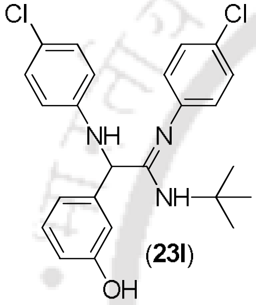
White solid, mp 188 °C; **IR** (KBr): 3401, 3371, 3045, 2961, 1634, 1599, 1513, 1494, 1482, 1182, 1089 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.58 (d, *J* = 6.4 Hz, 1H), 7.31-7.27 (m, 3H), 7.19 (dd, *J* = 6.8 Hz, *J* = 2 Hz, 2H), 6.97 (dd, *J* = 6.8 Hz, *J* = 2.4 Hz, 2H),



(23k)

6.59 (dd, *J* = 7.2 Hz, *J* = 2.4 Hz, 2H), 6.31 (dd, *J* = 6.4 Hz, *J* = 2 Hz, 2H), 5.90 (bs, 1H, NH), 5.16 (d, *J* = 2.0 Hz, 1H), 3.63 (bs, 1H, NH), 1.47 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 153.9, 149.1, 145.8, 136.8, 134.9, 130.2, 129.4, 129.1, 128.7, 127.4, 126.6, 124.7, 123.2, 115.0, 57.2, 51.4, 28.5. **Anal. Calcd** for $C_{24}H_{24}Cl_3N_3$ (460.83): C, 62.55; H, 5.25; N, 9.12. Found: C, 62.44; H, 5.16; N, 9.02.

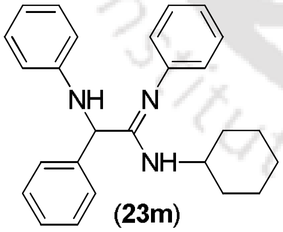
N-tert-Butyl-N'-(4-chlorophenyl)-2-(4-chlorophenylamino)2(3hydroxyphenyl)acetamidine (**23l**)



(23l)

Yellow solid, mp 192 °C; **IR** (KBr): 3384, 2964, 2924, 1630, 1597, 1586, 1493, 1484, 1454, 1251, 1089 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.17-7.10 (m, 3H), 6.99 (d, *J* = 8.4 Hz, 2H), 6.74 (d, *J* = 7.6 Hz, 1H), 6.65 (d, *J* = 7.2 Hz, 1H), 6.56 (s, 1H), 6.53 (d, *J* = 8.4 Hz, 2H), 6.40 (d, *J* = 8.4 Hz, 2H), 5.84 (bs, 1H, NH), 4.70 (s, 1H), 3.76 (bs, 1H, NH), 3.45 (bs, 1H, OH), 1.41 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 156.6, 154.3, 149.0, 145.5, 140.8, 130.4, 129.4, 128.6, 126.7, 124.5, 123.8, 120.0, 115.8, 115.0, 114.9, 60.0, 51.3, 28.5. **Anal. Calcd** for $C_{24}H_{25}Cl_2N_3O$ (442.38): C, 65.16; H, 5.70; N, 9.50. Found: C, 65.04; H, 5.58; N, 9.42.

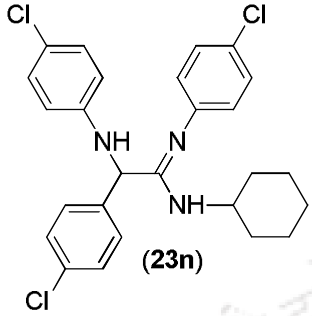
N-Cyclohexyl-N',2-diphenyl-2-(phenyl amino)acetamidine (**23m**)



(23m)

White solid, mp 148 °C; **IR** (KBr): 3373, 3238, 3023, 2928, 2853, 1621, 1589, 1517, 1495, 1484, 1313, 1259, 1199 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.28-7.22 (m, 5H), 7.12-7.05 (m, 4H), 6.85-6.80 (m, 2H), 6.69 (d, *J* = 8.0 Hz, 2H), 6.50 (d, *J* = 7.2 Hz, 2H), 5.97 (bs, 1H, NH), 4.97 (s, 1H), 3.94 (bs, 1H, NH), 2.13-2.05 (m, 2H), 1.45-1.40 (m, 4H), 1.30-1.07 (m, 5H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 155.2, 150.6, 147.2, 139.6, 129.3, 128.8, 128.5, 128.3, 128.1, 122.8, 121.6, 119.4, 113.8, 59.8, 48.6, 33.1, 32.6, 25.9, 25.0, 24.8. **Anal. Calcd** for $C_{26}H_{29}N_3$ (383.53): C, 81.42; H, 7.62; N, 10.96. Found: C, 81.32; H, 7.54; N, 10.88.

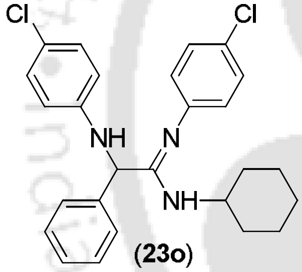
N',2-bis(4-Chlorophenyl)-2-(4-chlorophenylamino)-N-cyclohexylacetamidine (**23n**)



(**23n**)

Pale yellow, mp 148 °C; **IR** (KBr): 3255, 2934, 2855, 1640, 1600, 1492, 1256, 1091, 1013 cm^{-1}; ^{1}**H NMR** (400 MHz, $CDCl_3$/DMSO): δ 7.25 (d, *J* = 7.2 Hz, 2H), 7.18 (m, 4H), 6.99 (d, *J* = 6.8 Hz, 2H), 6.70 (d, *J* = 6.8 Hz, 2H), 6.56 (d, *J* = 7.6 Hz, 2H), 4.97 (s, 1H), 3.79 (bs, 1H, NH), 3.20 (bs, 1H, NH), 1.98 (bs, 1H), 1.74-1.53 (m, 5H), 1.36-1.15 (m, 5H); ^{13}**C NMR** (100 MHz, $CDCl_3$): δ 161.5, 142.8, 132.8, 132.5, 131.8, 131.4, 128.1, 128.0, 127.5, 127.4, 126.7, 121.4, 113.5, 56.2, 50.7, 29.2, 23.0, 22.6 **Anal. Calcd** for $C_{26}H_{26}Cl_3N_3$ (486.86): C, 64.14; H, 5.38; N, 8.63 Found: C, 64.05; H, 5.29; N, 8.57.

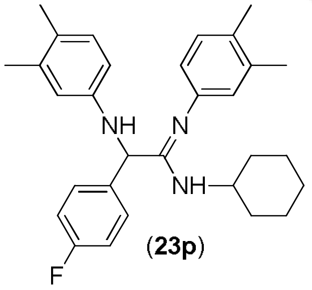
N'-(4-chlorophenyl)-2-((4-chlorophenyl)amino)-N-cyclohexyl-2-phenylacetimidamide (**23o**)



(**23o**)

White solid, mp 178 °C; ^{1}**H NMR** (400 MHz, $CDCl_3$): δ 7.31-7.26 (m, 3H), 7.16 (d, *J* = 8.4 Hz, 2H), 7.10 (d, *J* = 6.8 Hz, 2H), 6.99 (d, *J* = 8 Hz, 2H), 6.55 (d, *J* = 8.4 Hz, 2H), 6.38 (d, *J* = 8.4 Hz, 2H), 5.93 (d, *J* = 7.6 Hz, 1H), 4.83 (bs, NH, 1H), 3.85 (bs, NH, 1H), 2.11-1.97 (m, 2H), 1.72-1.61 (m, 3H), 1.45-1.03 (m, 6H); ^{13}**C NMR** (100 MHz, $CDCl_3$): δ 155.3, 148.9, 145.5, 138.8, 129.3, 129.1, 128.8, 128.6, 128.0, 126.9, 124.4, 124.0, 114.9, 59.9, 48.8, 33.1, 32.6, 25.8, 25.0, 24.9. **Anal. Calcd** for $C_{26}H_{27}Cl_2N_3$ (452.41): C, 69.02; H, 6.02; N, 9.29 Found: C, 68.94; H, 5.92; N, 9.21.

N-cyclohexyl-N'-(3,4-dimethylphenyl)-2-((3,4-dimethylphenyl)amino)-2-(4-fluorophenyl)acetimidamide (**23p**)



(**23p**)

Pale yellow solid, mp 175 °C; ^{1}**H NMR** (400 MHz, $CDCl_3$): δ 7.10-7.06 (m, 2H), 6.98-6.91 (m, 2H), 6.80 (d, *J* = 7.6 Hz, 1H), 6.50 (d, *J* = 2 Hz, 1H), 6.43 (dd, *J* = 8 Hz, *J* = 2.4, 1H), 6.25-6.22 (m, 2H), 5.93 (d, *J* = 8.4 Hz, 1H), 4.88 (bs, NH, 1H), 3.93-3.91 (m, 1H), 3.53 (bs, NH, 1H), 2.22 (s, 3H), 2.17 (s, 3H), 2.12 (s, 3H), 2.02 (s, 3H), 1.72-1.69 (m, 1H), 1.65-1.57 (m, 3H), 1.46-1.34 (m, 2H), 1.26-1.04 (m, 5H); ^{13}**C NMR** (100 MHz, $CDCl_3$): δ 155.6, 148.1, 145.4, 137.5, 136.4, 136.1, 130.4, 130.0, 129.7, 129.4, 127.6, 124.2, 119.8, 115.7, 115.5, 111.4, 59.5, 48.6, 33.3, 32.7, 26.0, 25.2, 25.0, 20.1, 19.8, 19.1, 18.9. **Anal. Calcd** for $C_{30}H_{36}FN_3$ (457.62): C, 78.74; H, 7.93; N, 9.18 Found: C, 78.63; H, 7.82; N, 9.05.

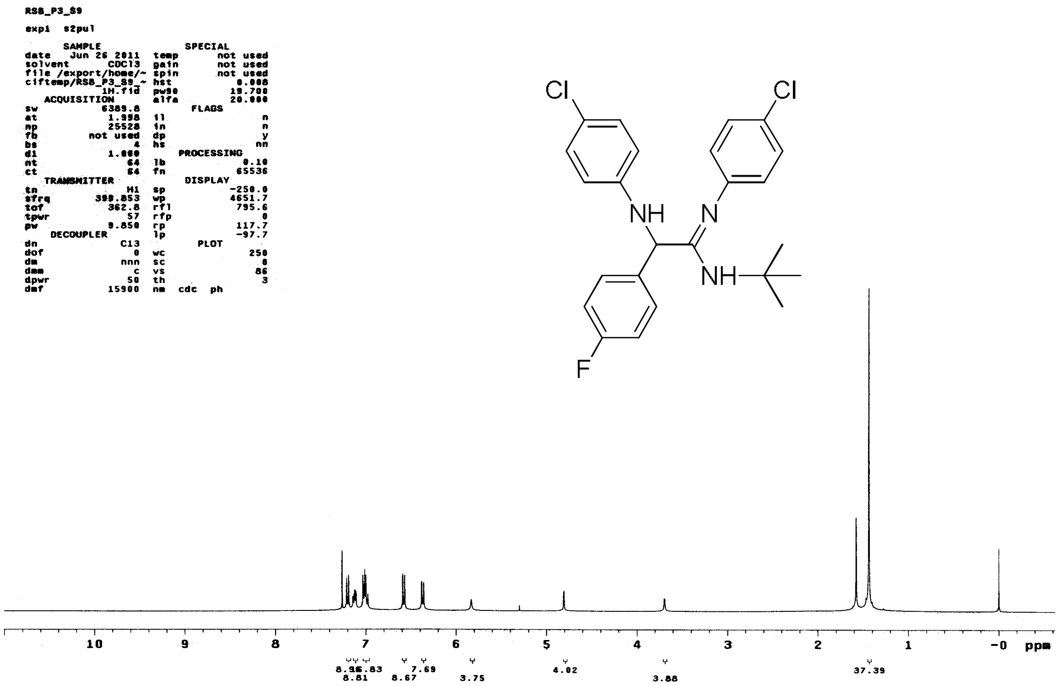
Complete crystallographic data of **23a**, **23b** and **23n** for the structural analysis have been deposited with the Cambridge Crystallographic Data Centre, CCDC No. 855248, 838468 and 837583 respectively. Copies of this information may be obtained free of charge from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK, (fax: +44-1223-336033, e-mail: deposit@ccdc.cam.ac.uk or via: www.ccdc.cam.ac.uk).

Table 14. Crystal data and structures refinement for the compound **23a, 23b** and **23n**, for atomic coordinates, equivalent isotropic displacement parameters and bond angles, please check the CIF.

Parameters	Compound **23a**	Compound **23b**	Compound **23n**
Empirical Formula	'$C_{24}H_{27}N_3$'	'$C_{24}H_{24}BrCl_2N_3$'	'$C_{26}H_{26}Cl_3N_3$'
Formula weight	357.49	505.27	486.85
Temperature	296 K	296 K	296 K
CCDC no	855248	838468	837583
Wavelength (Å)	0.71073 Å	0.71073 Å	0.71073 Å
Crystal system	Monoclinic	Orthorhombic	Monoclinic
Space group	P 21/c	Pna2(1)	P2(1)/n
Radiation type	Mo K\a	Mo K\a	Mo K\a
Radiation source	'fine-focus sealed tube'	'fine-focus sealed tube'	'fine-focus sealed tube'
a (Å)	11.6045 (7) Å	13.3588 (10) Å	12.9999 (9) Å
b (Å)	11.6974 (7) Å	10.7992 (8) Å	11.9658 (10) Å
c (Å)	15.6896 (10) Å	16.6412 (12) Å	16.7478 (12) Å
α (°)	90.00°	90.00°	90.00°
β (°)	102.044 (3)°	90.00°	92.120 (4)°
γ (°)	90.00°	90.00°	90.00°
Cell Volume	2082.9 (2) $Å^3$	2400.7 (3) $Å^3$	2603.4 (3) $Å^3$
Z	4	4	4

Density	1.140 g/cm^3	1.398 g/cm^3	1.242 g/cm^3
F(0 0 0)	768	1032	1016
Theta range for data collection	1.79 to 25.50°	2.25 to 28.44°	1.95 to 26.49°
Index ranges	-10<=h<=14, -13<=k<=13, -18<=l<=18	-17<=h<=17, -14<=k<=14, -22<=l<=22	-13<=h<=15, -13<=k<=12, -20<=l<=20
Reflections collected	20224	29277	21584
Independent reflections	3784 [R(int) = 0.1111]	5976 [R(int) = 0.0367]	4970 [R(int) = 0.0450]
Completeness to theta	25.50° 97.7 %	28.44° 99.6 %	26.49° 92.4 %
Number of parameters	247	271	289
Number of restraints	0	1	0
Goodness-of-fit (GOF) on F^2	0.973	0.993	1.031
Refinement method	Full-matrix least-squares on F2	Full-matrix least-squares on F2	Full-matrix least-squares on F2

^{1}H NMR (400 MHz, CDCl$_3$): *2-(4-Chlorophenylamino)-N-tert-butyl-N'-(4-chlorophenyl)-2-(4-fluorophenyl)acetamidine* (**23e**)



```
RSB_P3_S9

expl  s2pul

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solvent       CDCl3  gain       not used
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             1H.fid  pw90         19.700
   ACQUISITION       alfa         20.000
sw           6385.8        FLAGS
at            1.998  il                n
np            25528  in                n
fb         not used  dp                y
bs                4  hs               nn
d1            1.000      PROCESSING
nt               64  lb             0.10
ct               64  fn            65536
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tn               H1  sp           -250.0
sfrq        399.853  wp           4651.7
tof           362.8  rfl           795.6
tpwr             57  rfp               0
pw            9.850  rp            117.7
    DECOUPLER        lp            -97.7
dn              C13          PLOT
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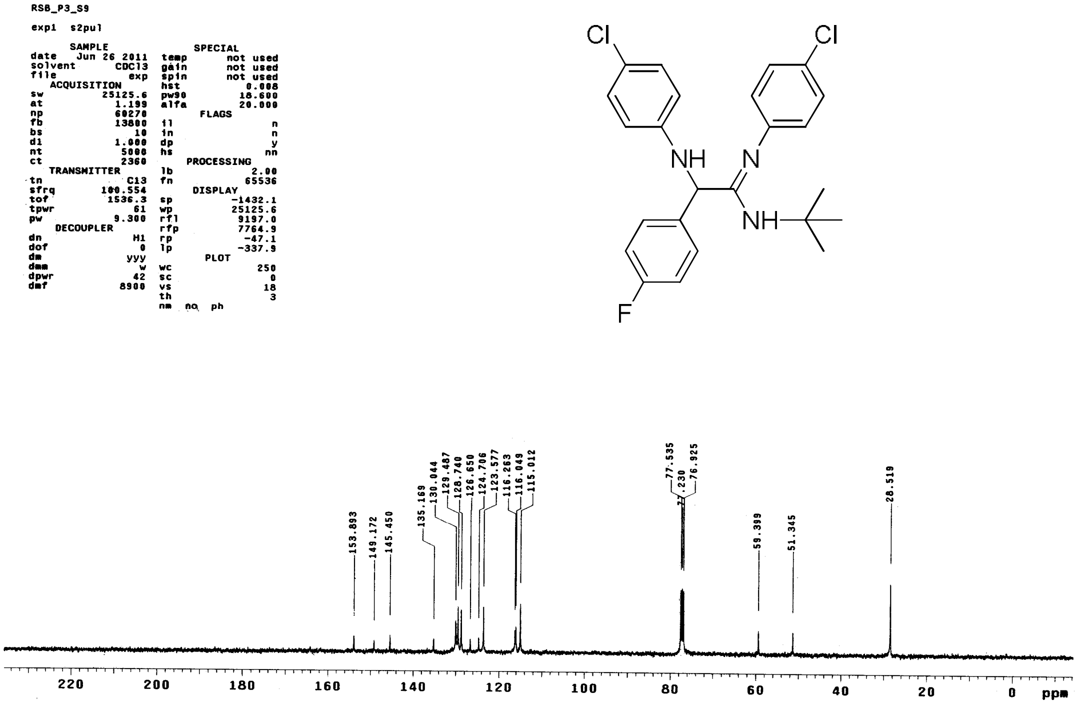
dm              nnn  sc                0
dmm               c  vs               86
dpwr             50  th                3
dmf           15900  nm  cdc  ph
```

^{13}C NMR (100 MHz, CDCl$_3$): *2-(4-Chlorophenylamino)-N-tert-butyl-N'-(4-chlorophenyl)-2-(4-fluorophenyl)acetamidine* (**23e**)



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RSB_P3_S9

expl  s2pul

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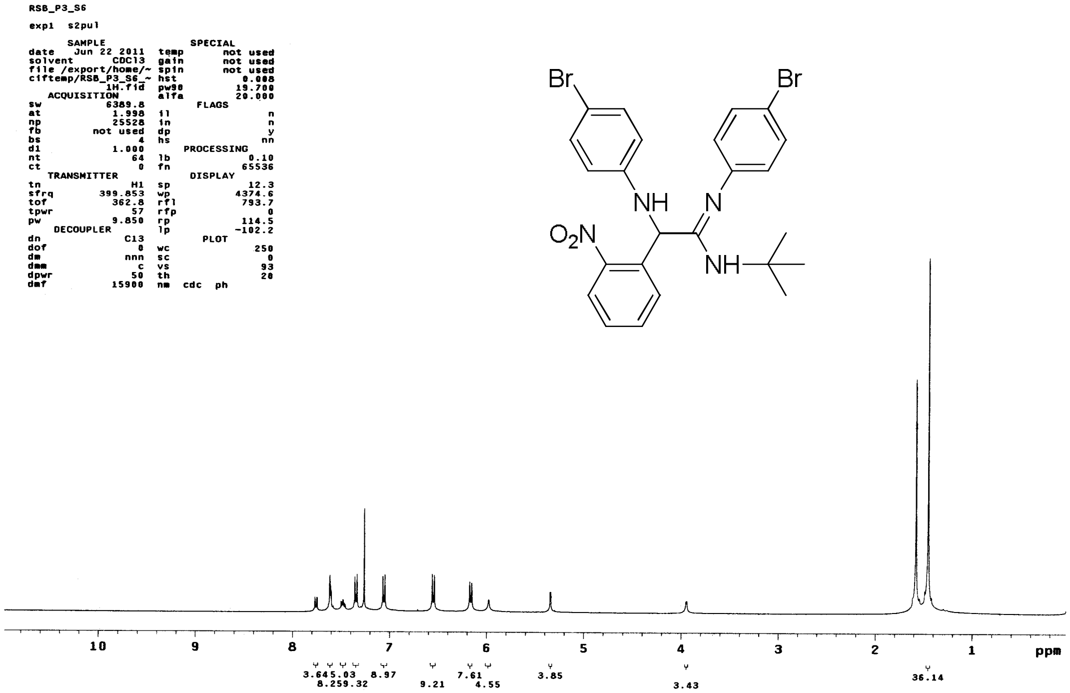
solvent       CDCl3  gain       not used
file            exp  spin       not used
   ACQUISITION       hst           0.008
sw          25125.6  pw90         18.600
at            1.199  alfa         20.000
np            60270        FLAGS
fb            13800  il                n
bs               10  in                n
d1            1.000  dp                y
nt             5000  hs               nn
ct             2360      PROCESSING
   TRANSMITTER       lb             2.00
tn              C13  fn            65536
sfrq        100.554       DISPLAY
tof          1536.3  sp          -1432.1
tpwr             61  wp          25125.6
pw            9.300  rfl          9197.0
    DECOUPLER        rfp          7764.9
dn               H1  rp            -47.1
dof               0  lp           -337.9
dm              yyy          PLOT
dmm               w  wc              250
dpwr             42  sc                0
dmf            8900  vs               18
                     th                3
                     nm  no  ph
```

***^{1}H NMR (400 MHz, CDCl$_3$)**: 2-(4-Bromophenylamino)-N-tert-butyl-N'-(4-bromophenyl)-2-(2-nitrophenyl)acetamidine* (**23h**)



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RSB_P3_S6

exp1  s2pul

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solvent      CDCl3  gain       not used
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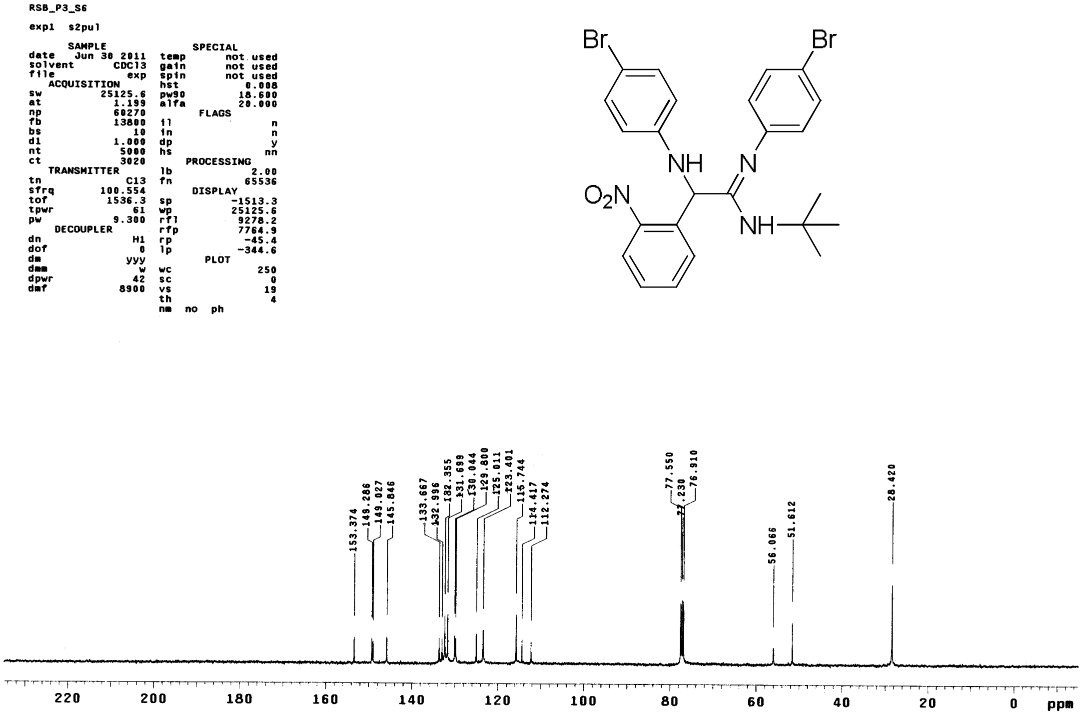
ciftemp/RSB_P3_S6_~ hst           0.008
            1H.fid  pw90         19.700
   ACQUISITION      alfa         20.000
sw          6389.8          FLAGS
at           1.998  il                n
np           25528  in                n
fb        not used  dp                y
bs               4  hs               nn
d1           1.000         PROCESSING
nt              64  lb             0.10
ct               0  fn            65536
   TRANSMITTER              DISPLAY
tn              H1  sp             12.3
sfrq       399.853  wp           4374.6
tof          362.8  rfl           793.7
tpwr            57  rfp               0
pw           9.850  rp            114.5
    DECOUPLER       lp           -102.2
dn             C13            PLOT
dof              0  wc              250
dm             nnn  sc                0
dmm              c  vs               93
dpwr            50  th               20
dmf          15900  nm   cdc   ph
```

***^{13}C NMR (100 MHz, CDCl$_3$)**: 2-(4-Bromophenylamino)-N-tert-butyl-N'-(4-bromophenyl)-2-(2-nitrophenyl)acetamidine* (**23h**)



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RSB_P3_S6

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solvent      CDCl3  gain       not used
file           exp  spin       not used
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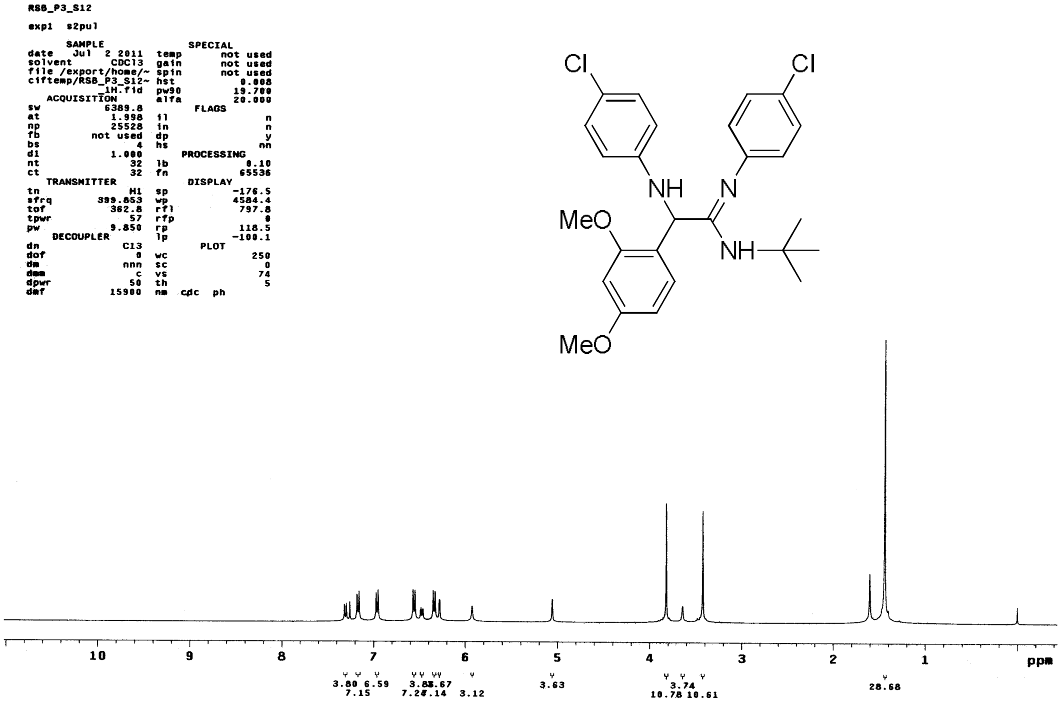
sw         25125.6  pw90         18.600
at           1.199  alfa         20.000
np           60270          FLAGS
fb           13800  il                n
bs              10  in                n
d1           1.000  dp                y
nt            5000  hs               nn
ct            3020         PROCESSING
   TRANSMITTER      lb             2.00
tn             C13  fn            65536
sfrq       100.554          DISPLAY
tof         1536.3  sp          -1513.3
tpwr            61  wp          25125.6
pw           9.300  rfl          9278.2
    DECOUPLER       rfp          7764.9
dn              H1  rp            -45.4
dof              0  lp           -344.6
dm             yyy            PLOT
dmm              w  wc              250
dpwr            42  sc                0
dmf           8900  vs               19
                    th                4
                    nm   no   ph
```

***^{1}H NMR (400 MHz, CDCl$_3$)**: 2-(4-Chlorophenylamino)-N-tert-butyl-N'-(4-chlorophenyl)-2-(2,4dimethoxyphenyl)acetamidine* (**23j**)



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RSB_P3_S12

exp1  s2pul

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solvent       CDCl3   gain      not used
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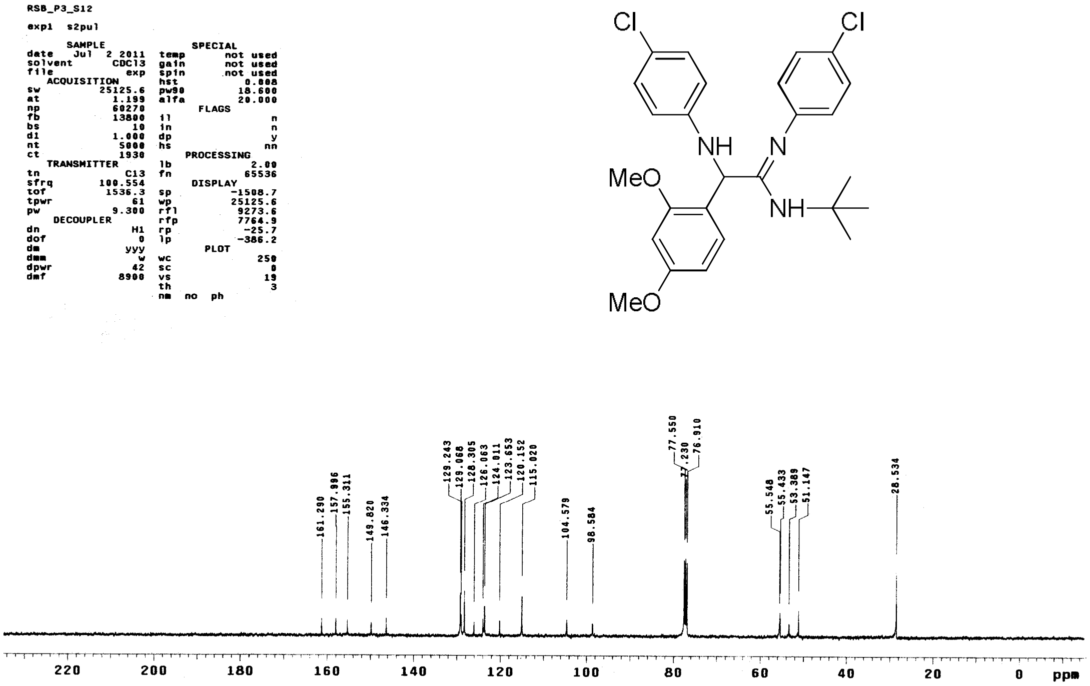
ciftemp/RSB_P3_S12~   hst          0.008
           _1H.fid    pw90        19.700
   ACQUISITION        alfa        20.000
sw           6389.8            FLAGS
at            1.998   il               n
np            25528   in               n
fb         not used   dp               y
bs                4   hs              nn
d1            1.000         PROCESSING
nt               32   lb            0.10
ct               32   fn           65536
   TRANSMITTER               DISPLAY
tn               H1   sp          -176.5
sfrq        399.853   wp          4584.4
tof           362.8   rfl          797.8
tpwr             57   rfp              0
pw            9.850   rp           118.5
    DECOUPLER         lp          -100.1
dn              C13              PLOT
dof               0   wc             250
dm              nnn   sc               0
dmm               c   vs              74
dpwr             50   th               5
dmf           15900   nm  cdc   ph
```

***^{13}C NMR (100 MHz, CDCl$_3$)**: 2-(4-Chlorophenylamino)-N-tert-butyl-N'-(4-chlorophenyl)-2-(2,4dimethoxyphenyl)acetamidine* (**23j**)



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RSB_P3_S12

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file            exp   spin      not used
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sw          25125.6   pw90        18.600
at            1.199   alfa        20.000
np            60270            FLAGS
fb            13800   il               n
bs               10   in               n
d1            1.000   dp               y
nt             5000   hs              nn
ct             1930         PROCESSING
   TRANSMITTER        lb            2.00
tn              C13   fn           65536
sfrq        100.554          DISPLAY
tof          1536.3   sp         -1508.7
tpwr             61   wp         25125.6
pw            9.300   rfl         9273.6
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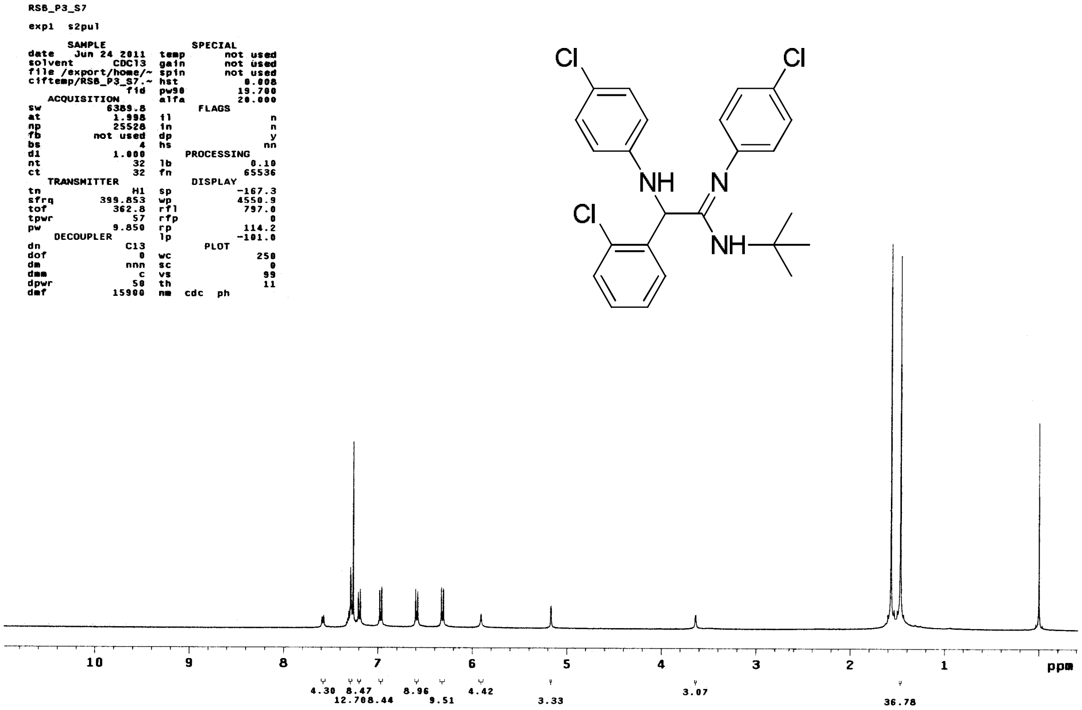
dn               H1   rp           -25.7
dof               0   lp          -386.2
dm              yyy              PLOT
dmm               w   wc             250
dpwr             42   sc               0
dmf            8900   vs              19
                      th               3
                      nm  no   ph
```

***^{1}H NMR (400 MHz, CDCl$_3$)**: 2-(4-Chlorophenylamino)-N-tert-butyl-2-(2-chlorophenyl)-N'-(4-chlorophenyl)acetamidine* (**23k**)



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RSB_P3_S7

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solvent      CDC13  gain       not used
file /export/home/~ spin       not used
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               fid  pw90         19.700
   ACQUISITION      alfa         20.000
sw          6389.8           FLAGS
at           1.998  il                n
np           25528  in                n
fb        not used  dp                y
bs               4  hs               nn
d1           1.000         PROCESSING
nt              32  lb             0.10
ct              32  fn            65536
   TRANSMITTER             DISPLAY
tn              H1  sp           -167.3
sfrq       399.853  wp           4550.9
tof          362.8  rfl           797.0
tpwr            57  rfp               0
pw           9.850  rp            114.2
    DECOUPLER       lp           -101.0
dn             C13            PLOT
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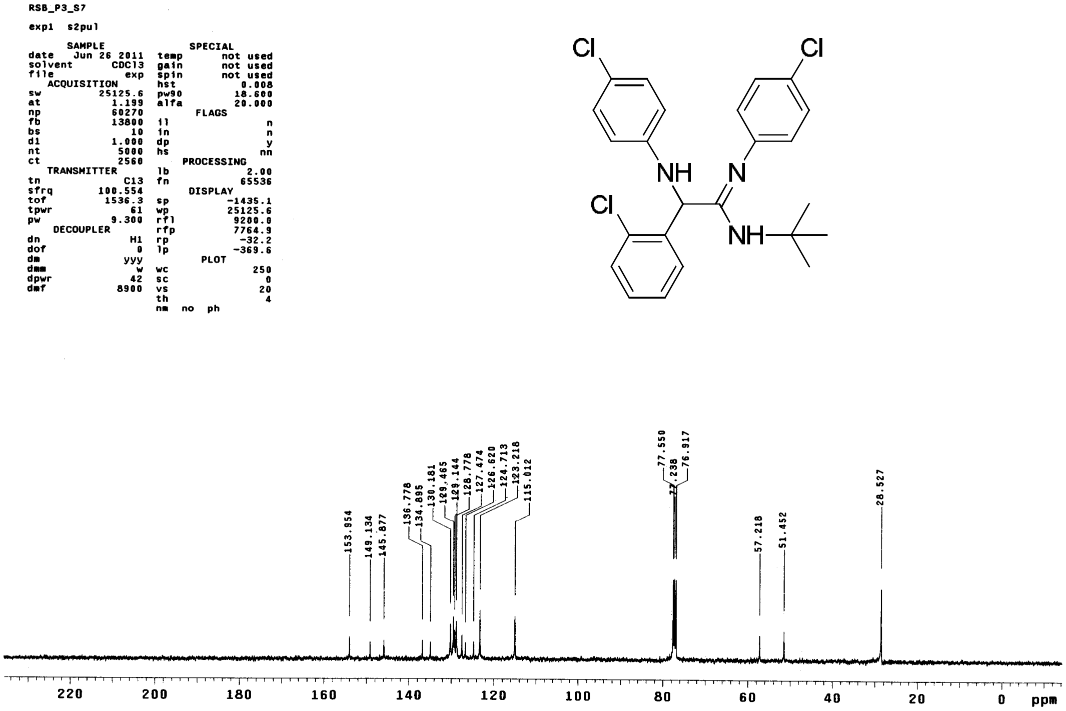
dm             nnn  sc                0
dmm              c  vs               99
dpwr            50  th               11
dmf          15900  nm  cdc  ph
```

***^{13}C NMR (100 MHz, CDCl$_3$)**: 2-(4-Chlorophenylamino)-N-tert-butyl-2-(2-chlorophenyl)-N'-(4-chlorophenyl)acetamidine* (**23k**)



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RSB_P3_S7

exp1  s2pul

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sw         25125.6  pw90         18.600
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d1           1.000  dp                y
nt            5000  hs               nn
ct            2560         PROCESSING
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tn             C13  fn            65536
sfrq       100.554         DISPLAY
tof         1536.3  sp          -1435.1
tpwr            61  wp          25125.6
pw           9.300  rfl          9200.0
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dn              H1  rp            -32.2
dof              0  lp           -369.6
dm             yyy            PLOT
dmm              w  wc              250
dpwr            42  sc                0
dmf           8900  vs               20
                    th                4
                    nm  no  ph
```

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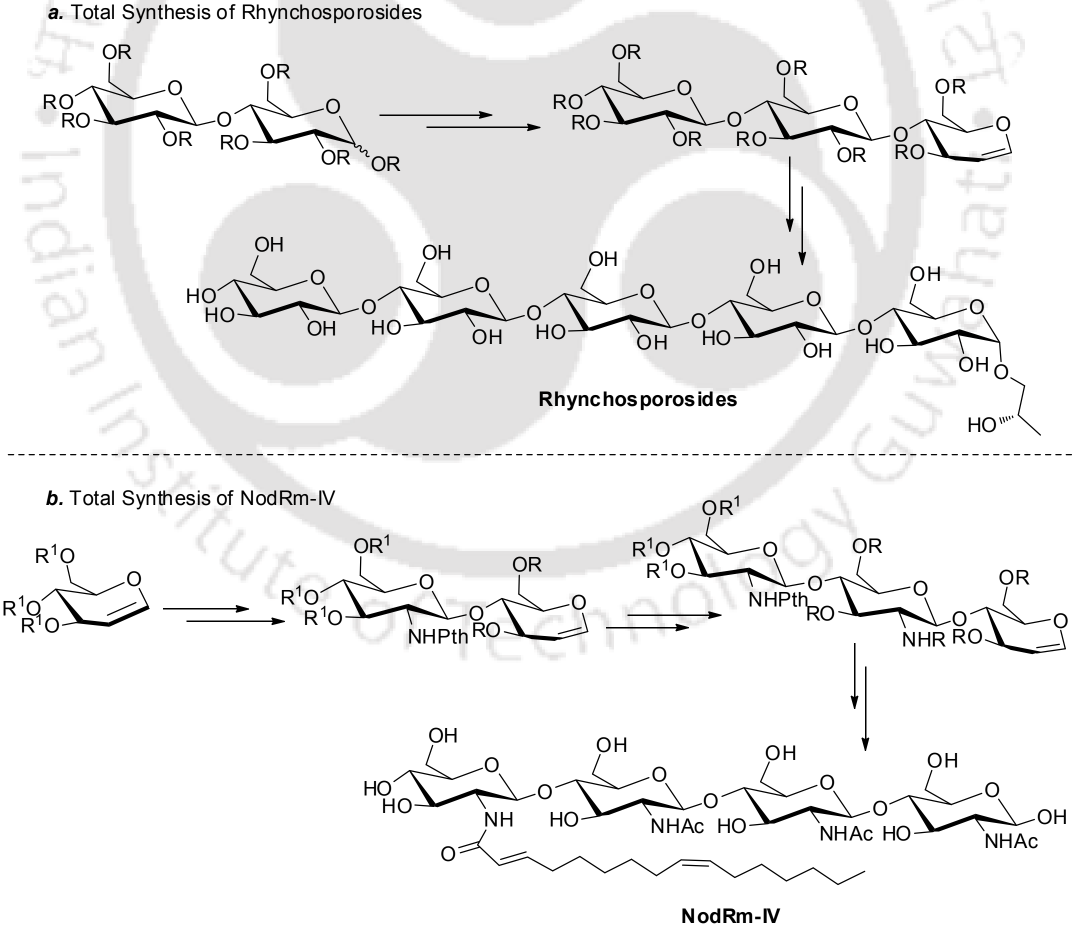
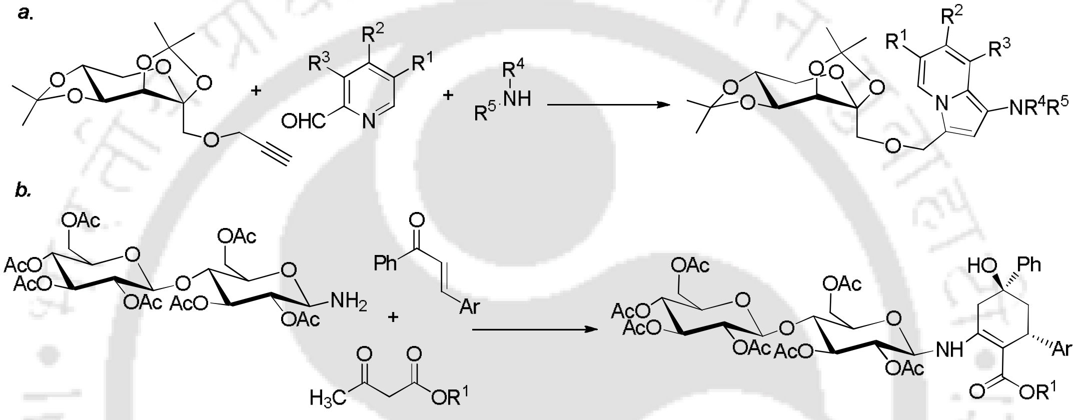
Conclusion and Future Perspectives

Over all, the thesis describes a new methodology for the synthesis of 2-deoxy-2-iodo-*O*-glycosylation using *in situ* generated iodonium ion catalyzed by oxobis(acetylacetonato) vanadium. Furthermore, we have explored BDMS as a catalyst, in carbohydrate chemistry and in multicomponent reaction to deliver a new methodology for the synthesis of 2,3-unsaturated-*O*-glycoside, imidazo[1,2-*a*]pyridine and α-aminoamidine. Besides that, we believe 2-deoxy-2-iodo-*O*-glycoside approach can be extensively utilized for target-oriented synthesis of natural products in modern organic synthesis. Indeed, 2,3-unsaturated-*O*-glycoside were further used as a synthetic intermediate for targeted complex natural products and as asymmetric catalyst in near future. Moreover, the synthesized imidazo[1,2-*a*]pyridine and α-aminoamidine can be explored for biological studies.



Scheme 1

The knowledge gathered from the output of 2-iodo-*O*-glycosylation synthesis spurred us to work on target-oriented synthesis. In future, we will try to achieve the total synthesis of Rhynchosporosides from cellobiose through *O*-glycosylation. In addition to that, we will try to achieve the target NodRm-IV from glucal and their retrosynthetic representation is shown in Scheme 1. Synthetic chemists are keen to generate sugar-based library of molecules for drug design in near future. In this regard the future endeavor would be to achieve the sugar based multicomponent reaction as shown in Scheme 2.



Scheme 2

List of Publications

1. *‘$VO(acac)_2/H_2O_2/NaI$: a mild and efficient combination for the cleavage of dithio acetal derivatives of sugars’* Abu T. Khan*, Shahzad Ali, **R. Sidick Basha**, Md. Musawwer Khan and Mohan Lal, *Carbohydr. Res.* **2011**, *346*, 2629-2632.

2. *‘Bromodimethylsulfonium bromide (BDMS) catalyzed synthesis of imidazo[1,2-a]pyridine derivatives and their fluorescence properties’* Abu T. Khan*, **R. Sidick Basha** and Mohan Lal*, Tetrahedron Lett.* **2012**, *53,* 2211-2217.

3. *‘Formation of unexpected α-amino amidine through three-component ‘UGI condensation reaction’* Abu T. Khan*, **R. Sidick Basha**, Mohan Lal and Mohammad Hedayetullah Mir, *RSC Adv.,* **2012***, 2,* 5506-5509.

4. *‘Synthesis of tetra-substituted pyrroles, a potential phosphodiesterase 4B inhibitor, through nickel(II) chloride hexahydrate catalyzed one-pot four-component reaction’* Abu T. Khan*, Mohan Lal, Prasanta Ray Bagdi, **R. Sidick Basha**, Parameswaran Saravanan and Sanjukta Patra*, Tetrahedron Lett.* **2012***, 53,* 4145-4150. *(Recognized as one of the Top 25 most downloaded article July’12-Sep’12).*

5. *‘Bromodimethylsulfonium bromide (BDMS) catalyzed synthesis of 2,3-unsaturated-O-glycosides via Ferrier rearrangement’* Abu T. Khan*, **R. Sidick Basha** and Mohan Lal, *ARKIVOC* **2013** (ii) 201-212. *(Special Issue in honor of Prof Richard R. Schmidt).*

6. *‘Synthesis of Trisubstituted 1H-Pyrazole-4-carbodithioates in a One-Pot Three-Component Reaction Catalyzed by Ferric Sulfate’* Abu T. Khan*, Arindam Ghosh, **R. Sidick Basha** and Mohammad Hedayetullah Mir, *Asian J. Org. Chem.* **2013**, *2*, 126-129. *(Featured as editor choice spotlight article).*

7. *'Regio- and diastereoselective synthesis of trans-2,3-dihydrofuran derivatives in an Aqueous medium'* Abu T. Khan*, Mohan Lal and **R. Sidick Basha**, *Synthesis* **2013***, 45*, 406-412.

8. *'Cobalt triflate catalyzed one-pot Synthesis of fluorophore 1,4-Dihydropyridine derivatives via Hantzsch Reaction'* Prasanta Ray Bagdi, **R. Sidick Basha**, Mohan Lal, Rajkumar Misra and Abu T. Khan,* *J. Indian Chem. Soc.,* **2013**, *90,* 1589-1598. *(Special Issue in honor of Prof. Sunil Kumar Talapatra).*

9. *'Bromodimethylsulfonium bromide (BDMS)-catalyzed synthesis of substituted pyrroles through a one-pot four-component reaction'* Prasanta Ray Bagdi, **R. Sidick Basha**, Mohan Lal, and Abu T. Khan,* *Chem. Lett.* **2013***, 42,* 939-941.

10. *'2,6-Pyridinedicarboxylic acid as organocatalyst for the synthesis of 1,5-benzodiazepines through one-pot reaction'* Mohan Lal, **R. Sidick Basha**, Satavisha Sarkar and Abu T. Khan,* *Tetrahedron Lett.* **2013**, *54,* 4264-4272.

11. *'Copper oxide nanoparticle mediated 'click chemistry' for the synthesis of mono-bis- and tris-triazole derivatives from 10,10-dipropargyl-9-anthrone as a key building block'* Prasanta Ray Bagdi, **R. Sidick Basha**, Pranjal Kumar Baruah and Abu T. Khan,* *RSC Adv.*, **2014**, *4,* 10652-10659.

12. *'Aqueous Biphasic Mediated Stereoselective Synthesis of 2-deoxy-2-iodo-O-glycoside through in situ generated Iodonium ion Catalyzed by Oxobis(acetylacetonato)vanadium'* **R. Sidick Basha** and Abu T. Khan* (Manuscript under preparation).

13. *'Copper oxide nanoparticle catalyzed synthesis of 3-substituted-2-(1-alkyl-1,2,3-triazol-4-yl)-imidazo[1,2-a]pyridine derivatives in one-pot three component reaction'* Prasanta Ray Bagdi, **R. Sidick Basha** and Abu T. Khan* (Communicated).

14. ‘*Synthesis of 1,4-di-substituted bis-triazole derivatives in one-pot three component reaction catalyzed by Copper oxide nanoparticle’* Prasanta Ray Bagdi, **R. Sidick Basha** and Abu T. Khan* (Manuscript under preparation).

15. *‘Synthesis and characterization of Symmetrical and Unsymmetrical Vanadium salen complexes’* **R. Sidick Basha**, Prasanta Ray Bagdi and Abu T. Khan* (Manuscript under preparation).